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THE JOURNAL

OF THE

American Medical Association

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association. Subscription price, $15.00 a year, 45c a copy. Canadian $16.50. Foreign $19.00. Entered as second class matter June 25, 1885, at the Postoffice at Chicago, Ill., under act of March 3, 1879. Address all communications to
American Medical Association, 535 N. Dearborn St., Chicago 10, Illinois

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THE JOURNAL
of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 154, NO. 1 CHICAGO, ILLINOIS JANUARY 2, 1954
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TREATMENT OF MALIGNANT CUTANEOUS LESIONS

Earl D. Osborne, M.D., Buffalo, N. Y.

Statistical evaluation of results in the treatment of malignant cutaneous lesions is scientifically impossible. Except for superficial small epitheliomas on fairly smooth areas of glabrous skin, all lesions differ in some respect. In deciding the method of treatment in any particular case, the following factors must be considered: 1. The age and general condition of the patient, including the mental status. With many patients, it is desirable to treat the lesion when the patient is first seen. This is especially true when an emotional anxiety state caused by diagnosis of cancer exists. Elderly infirm patients are frequently unable to carry out a protracted schedule of treatment. 2. The accessibility of the patient to proper treatment. When he must travel long distances from home to office or clinic, two to seven trips a week are often impossible. If a one treatment method is available, with results comparable to any other method, the single treatment should be the method of choice. 3. The anatomic location of the malignant lesion. This is important from several viewpoints. The cosmetic result from treatment is sometimes of paramount importance, more so in females than in males. The first thought must always be to use the method of treatment that will yield the highest percentage of cures with the least disturbance in the continuity of tissue. It is at this point that many differences of opinion are expressed. Many of these disagreements are the result of bias and unfamiliarity with methods other than the favorite method of the sponsor.

Certain methods of treatment, which produce an apparent excellent cosmetic result, 5 or 10 years later give rise to disfiguring sequelae that are difficult and sometimes impossible to repair. Cosmetic appearance and the maintenance of structural continuity should never be considered paramount to the histological cell type of growth. If microscopic study reveals immaturity and infiltration, the question of cosmetic appearance should be entirely secondary to the cure of the patient. This consideration often applies to lesions contiguous to or in continuity with mucous membrane surfaces of the mouth, nose, eyelids, anogenital area, and ears. Wholly inadequate methods are often used in such circumstances, particularly superficial radiation therapy of a fairly early infiltrating immature squamous cell epithelioma at any mucocutaneous junction, or surgical removal of an infiltrating basal cell epithelioma on the nose, the ala nasi, or the adjacent upper lip, where pseudopods are sometimes present. In cutting across the pseudopods, a deep, infiltrating recurrence results, which is difficult and occasionally impossible to cure. In these cases, a destructive form of therapy must be used to give the patient the best chance of survival, irrespective of the immediate cosmetic result. Later, if it is necessary, plastic repair can produce a satisfactory cosmetic result. In handling cases showing an early infiltrating immature squamous cell epithelioma, the initial treatment is usually the deciding point of success or failure. If the physician is irresolute and administers an ineffectual treatment, it is sometimes too late to accomplish a cure afterward. Proximity of the lesion to cartilage, tendon, and bone must always be considered. Although some good results have been secured with radiation treatment over cartilage, bone, and tendon, generally speaking, wide scalpel surgery or electrosurgery, produce the best results. This question is closely related to the factor of adequate blood supply to promote healing after treatment. There are many areas on the body over cartilage, tendon, and bone where a cancerocidal dose of radiation may lead to long-continued necrosis and ulceration, with failure to heal for many months.

The ability of the patient to pay should never be a consideration in the treatment of any form of malignant cutaneous lesion. Potentially metastasizing lesions should always be treated by the method or combination of methods judged most likely to result in cure. Fortunately, the vast majority of cutaneous lesions are superficial and benign and can be cured in a number of ways, including scalpel surgery, electrosurgery, chemosurgery, and radiation. Without any demonstrated scientific superiority in results, the use of a modern operating room, with or without a hospital bed, in the handling of the ordinary uncomplicated noninfiltrating basal cell epithelioma is unwarranted and uneconomical, and results in unnecessary expense for the patient. Treatment of equal or superior value can be administered in the office or clinic.

Read in the Symposium on Cutaneous Malignancy, an Appropriate Segment of Dermatology, before the Section on Dermatology and Syphilology at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

CURETTAGE AND BIOPSY

By training and experience, the dermatologist is superlatively qualified to recognize the earliest changes of malignant cutaneous lesions. The early recognition of a minute pearly nodule, with telangiectasia and a faintly raised pearly border, and the palpation of a small infiltrating nodule are part of the diagnostic acumen of any well-trained and experienced dermatologist. Curettage of large numbers of lesions, both nonmalignant and malignant, adds greatly to diagnostic acuteness. The proper use of the curette, both in diagnosis and treatment, yields information that can be obtained in no other way. Any method of treatment that employs preliminary curettage affords the operator valuable information regarding the depth of the lesion, especially in pockets and in lateral extensions, and it is exceedingly valuable in determining the extent of destructive treatment. This is especially applicable when using electrosurgery or chemosurgery. One of the valid criticisms of scalpel surgery and any form of radiotherapy is that not enough information is available regarding the exact extent of the lesion. I have seen many examples of the importance of this factor in failures from treatment, both in my patients and in the patients of others. Scalpel surgery may cut across lateral extensions or miss deep pockets, whereas in radiation therapy the proper quality of radiation is not used, and the depth dose is not sufficient. With radium needles, accuracy of application cannot be accomplished.

A microscopic study of biopsy material is indispensable; however, the blind acceptance of a negative report of one specimen of tissue may sometimes lead to disaster. Through no fault of the pathologist, the percentage of error from examination of a single specimen is between 5 and 10%. Within one week, I had the frightening experience of having two biopsy specimens, taken by an experienced person, from two patients with typical early squamous cell epitheliomas of the lower lip, reported back by the pathologist as nonmalignant. There is no substitute for clinical experience and diagnostic acumen possessed by the dermatologist in handling dangerous early metastasizing epitheliomas. Too often, valuable time is lost waiting several weeks for a second biopsy and a microscopic diagnosis.

In addition to the above-mentioned mucocutaneous lesions, there are two other early metastasizing lesions in the diagnosis of which sole reliance on a single biopsy specimen, and in some cases several biopsy specimens, may have tragic consequences; for example, in cases of Paget's disease of the nipple, biopsy must always include a segment of the nipple itself, down through the full thickness of the nipple. Biopsies of skin areas are notoriously apt to give negative results insofar as malignancy is concerned. The second lesion in this category is the very early development of malignant melanoma in a pigmented nevus. Pathologists are well aware of their inability to distinguish the line between nonmalignancy and malignancy and, of necessity, tend to err on the side of positive malignancy. Here again, dermatologists can be extremely valuable in clinically recognizing the localized, faint, translucent, pearly border of malignant change. Because of early metastasis with a fatal outcome, suspected lesions should always be widely removed, irrespective of a negative microscopic examination of a single piece of tissue, I have never seen a case in which biopsy could be incriminated as the cause of metastasis. The normal movements of the tissues plus the inevitable trauma of everyday life are of greater importance.

TYPES OF THERAPY

The straight scalpel treatment of malignant cutaneous lesions has its advocates among surgeons, especially the cancer surgeon, and some dermatologists. This resurgence in favor of scalpel surgery has been brought about through the teachings of wide excision of the primary lesion and operations in continuity to remove lymphatics, regional glands, and other structures. Finally, some surgeons maintain that wide excision, followed by plastic repair, maintains greater functional integrity and secures a better cosmetic result. Most cancer specialists today will readily admit that there is a large place for radical surgery in all cases of radioresistant tumors, such as malignant melanoma, Paget's disease of the breast, or where bone or cartilage are involved. There are, however, many expert radiologists and dermatologists who will not concede that radical surgery is routinely indicated in cases of radiosensitive tumors, in which the percentage of cure with radiation is equivalent to that of surgery. It is the author's opinion that radical surgery has its place in properly selected cases but that it has no demonstrable superiority over properly applied radiation in radiosensitive tumors. Scalpel surgery should always be used when wide removal of a primary lesion is advisable, as in the case of malignant melanoma, Paget's disease of the breast, large destructive basosquamous cell epitheliomas of the external ear, or lesions located over bone, cartilage, or tendon, which may yield very slow-healing chronic ulcers, when treated with radiotherapy, electrothermic destruction, or chemotherapy. This applies to lesions of the scalp and forehead and many fairly large lesions on the hands and feet and over other bony cartilaginous prominences. For the vast majority of lesions, however, other methods of treatment yield comparable and frequently superior results, with less risk of recurrence and entirely satisfactory cosmetic results, at far less expense. Scalpel surgery inevitably has failures in the same type of case in which it had failures 30 years ago. Pseudopods and infiltrating strands of malignant cells will be cut across, and deep recurrent infiltrating nodules will result, presenting serious problems in treatment. These cases are becoming commoner.

Electrothermic destruction, in which electrodesiccation, coagulation, and cautery are used, has had its advocates for more than 40 years. This method of treatment has the following advantages: 1. It can be used immediately in most cases, which is of great importance in handling elderly infirm persons and those coming from long distances. 2. It is a simple office or clinic procedure for the majority of cases and, therefore, relatively inexpensive. 3. Operative complications are at a minimum, since nearly all patients are ambulatory and fairly free of pain and discomfort. 4. Because of accuracy of employment and the combined use of the curette, the percentage of cures is at a maximum. The late cosmetic results are excellent, except in a small percentage of cases. In some cases hypertrophic scars result, which can and should be treated with radiation. In exten-

sive deep lesions, when disfiguring contractile scars are produced knowingly, plastic repair can be accomplished after sufficient time has elapsed to be certain of cure. In some lesions, the use of the flat cautery is superior to other methods, particularly in the large flat superficial basal cell epithelioma, occurring either singly or in large numbers. After curettage, with an exact outline of the advancing border, an ironing out of the lesion with a blunt cautery is extremely accurate. Destruction through the full thickness of the corium is unnecessary in many cases, and a thin atrophic scar results.

During the past 2 years, I have been comparing the late 5 and 10 year cosmetic results obtained with electrothermic treatment with a similar group of lesions treated with radiation 5 to 10 years before. While it must be admitted that in many cases radiation yielded remarkable cosmetic results, nevertheless, there are too many late sequelae from radiation that counterbalance the apparently fine cosmetic results from this therapy and that end in atrophy, telangiectasia, and possibly ulceration 5 or 10 years later. From the literature and from personal experience, it is evident that in approximately 5% of patients treated with radiation there is some degree of late necrosis even in the most competent hands. It must be admitted that radiodermatitis presents a more formidable problem than does a hypertrophic scar of similar extent. In lesions in which radiation or electrothermic methods can be used with equal curative results, in the long run, electrothermic methods are superior. The disadvantages of electrothermic treatment of malignant cutaneous lesions include: (1) pain of a local anesthetic; (2) discomfort of a healing wound; and (3) the production of some degree of scarring, which is often, with the lapse of time, unnoticeable.

Chemotherapy of malignant cutaneous lesions, as developed by Moh, and more recently modified by Lunsford and Allington, offers, theoretically, a superior method of treatment for most of these lesions, except when wide surgical removal is indicated. There is no question that microscopic control of destructive treatment has yielded results in many cases of serious infiltrating epithelioma that were unobtainable by any other method; however, use of this method, with its painstaking, time consuming elements, seems entirely unnecessary in the routine handling of most malignant cutaneous lesions. It seems to be applicable to less than 5% of the epitheliomas seen in office and clinic practice. It should be of value in all types of recurrent epitheliomas, especially those involving the nose, ala nasal folds, upper lip, and infiltrating lesions about the orbit. If the modification of Moh's method, as proposed by Lunsford and Allington, proves practical, it is a method that should be available to all medical centers.

The use of x-rays has been extremely popular in the treatment of malignant cutaneous lesions for more than 40 years. Dr. Lyle Kingery, at the University of Michigan, was the first to call attention to the advantages of saturation treatment. X-ray therapy had a great fall in popularity during the 1920's for various reasons which may be summarized as follows. 1. The single or double dose method of treatment was found inadequate in too large a percentage of cases. Also, intervals of one to four weeks between treatments, while suppressing the growth, failed to cure in a high percentage of cases. This type of treatment also led to late severe radiodermatitis. 2. Many lesions were found to be radioresistant to the technique used. 3. Too many physicians had x-ray machines, but not much experience in treating malignant cutaneous lesions. Although many excellent results were secured, especially by wise and experienced persons, the results on the whole were not satisfactory. This led to the widespread use of electrothermic methods in many centers, which, as pointed out above, have many points of superiority over other methods at the present time.

After Coutard, the saturation method of treatment became popular in 1934 and 1935, and since that time many modifications have been adopted. I have used most of the varying techniques, from daily treatment for 13 days and 39 $\frac{\infty}{r}$ units, to biweekly treatments for 4 weeks, or 8 treatments for a total of 8,000 r. In analyzing my results over a 15 year period, I have come to the following conclusions. 1. There must be a careful estimation of the extent and depth of each lesion. The size of the field and the quality of radiation must be gaged accordingly. Radiation with a half value layer of less than 1 mm. Al should not be used for lesions estimated to extend, at any point, more than 2 mm. below the surface. There are, at present, too many physicians using the same quality of superficial radiation for all malignant cutaneous lesions. 2. The total dose must vary, depending on the size of the lesion, the quality of radiation, and the time over which the saturation is maintained. It is my definite opinion that frequent treatments in an optimum period of approximately three weeks yield not only the best immediate results but also the most enduring late results, without disastrous sequelae. Twenty treatments in 20 days, with a total of 6,000 r yield better results than 10 treatments in 10 days of 6,000 r, or 4 treatments in 10 days of 1,500 r each for a total of 6,000 r. Individual doses of more than 600 r for a total of more than 5,000 r will cause considerably more atrophy and telangiectasia at the end of 5 or 10 years than will the same total dosage given in daily increments of 400 r. It is apparent that individualization of cases is necessary. When x-ray therapy is used, the patient must be accessible for at least three or four days a week for a period of two to four weeks. That any deviation from a schedule inevitably reduces the percentage of cures is a serious criticism, which rightly or wrongly discredits the method when results are analyzed. 3. X-ray therapy is, in most instances, unsurpassed in results by any other form of treatment for infiltrating lesions that are radiosensitive. This is particularly true in infiltrating basal or squamous cell lesions about the head and neck, in which any type of surgery results in disfigurement, but in which radiation, in expert hands, yields a high percentage of cures, with far more acceptable cosmetic results. In this group of cases, however, the most violent debate rages as to the method of choice. The surgeons favoring use of the scalpel, wide excision, and when necessary, an operation removing the draining lymphatics and regional nodes in continuity, maintain that this is the most rapid method, gives the highest percentage of cures, and in the long run, with plastic surgery, leaves less disfigurement. Those who advocate electrothermic methods maintain that the immediate destruction of the primary growth,

without any possibility of seeding and recurrent deep nodules that follow scalpel surgery, is the method of choice. Competent radiologists and dermatologists maintain that their curative results are just as high, with less mutilation, hospital expense, and time lost from work. Only time and experience will settle this problem.

The use of x-rays, even in the most experienced hands, has the disadvantages that (1) the patient must be accessible for two to four weeks; (2) occasionally the extent and depth of the lesion cannot be estimated, even by the most expert; and (3) disastrous late sequelae occur in a definite percentage of persons and sometimes when least expected.

The use of low intensity radium needles in the interstitial treatment of malignant cutaneous lesions is extremely popular in some parts of the United States, particularly in the Southwest and is frowned upon in other places. The use of 1 and 2 mg. needles with a high percentage of gamma radiation allows an entirely different technique than that of the old high intensity needles. The proponents of this method claim superiority of the method for patients who come long distances and who must return home after not more than one day's absence. They are then able to return in seven or eight days for removal of the needles. For farmers and ranchers, this offers an ideal method. The low intensity needles, with a high gamma ray output, have eliminated acute necrotizing reactions, produced a homogeneity of radiation in a controlled field, and eliminated to a large extent damage to cartilage, tendons, and bones. In the hands of the experts, there are many satisfactory results, and Martin has obtained superior results in all types of infiltrating carcinoma and lymph node metastasis. Those experienced in treating cancer with radiation, who oppose this method, do so because (1) their patients are accessible for two to four weeks, (2) they believe that everything that can be achieved with interstitial radiation can be achieved through the external application of x-rays, and (3) they feel that x-ray therapy can be more accurate in extent and depth than therapy with interstitial radiation.

SUMMARY AND CONCLUSIONS

It is evident that there are a number of methods for the treatment of malignant cutaneous lesions that have their advocates and opponents. Each method has its particular field of usefulness, and each method also has its limitations and restrictions. The expert will employ the method that, in his hands, yields the most rapid, sure, and least discomforting form of treatment. In the long run, it is the individual physician, and not the particular method, that is of greatest importance. It must also be true that violent espousal of one method of treatment to the almost complete exclusion of other methods of treatment is not warranted or justified by the facts.

In my opinion, in the majority of malignant cutaneous lesions, the use of thorough curettage followed by electrothermic destruction is favored, whenever possible, over all other methods, because (1) curettage is extremely valuable, not only in diagnosis but in determining depth and extent of the lesion; (2) results are immediate, requiring a minimum of visits to the office or clinic; (3) when necessary, plastic repair can be performed 6 to 12 months later; and (4) the late 5 and 10 year results are excellent.

There are special indications for the use of scalpel surgery, such as in Paget's disease of the breast, malignant melanoma, and other cases in which operations in continuity with draining lymphatics are desirable. There are also special indications for radiation therapy, especially in the case of radiosensitive malignant lesions that are infiltrating and when cosmetic results are of paramount importance. Local chemotherapy is especially valuable in selected cases.

71 North St.

RADIUM IN MALIGNANT CUTANEOUS DISEASE

C. F. Lehmann, M.D.
and
J. L. Pipkin, San Antonio, Texas

Radium may be used in treating skin cancer in the form of a pack or plaque or in the form of needles applied interstitially. The use of the packs (or plaques) has no advantage except in rare instances and will not be discussed. It is our opinion that radium used for malignant cutaneous disease serves best when used in needles applied into the lesion.

We have used two interstitial techniques with needles for a number of years, namely, (1) a short-time high-intensity method and (2) a long-time low-intensity method. The first has been described in a previous article [1] and will be discussed only briefly here. The short-time high-intensity technique (fig. 1) refers to the use of needles containing 10 mg. of radium, 19 mm. in length, with a wall filtration of 0.3 mm. of platinum. Their active length is 12 mm. These are inserted at the base of a skin cancer and usually placed 3 mm. apart. They are arranged in the following ways:

1. They can be arranged in a triangle about the border of small lesions. 2. They can be arranged through and through a small tumor at its base. Sometimes the skin underlying the ends of the needles is protected with a half-moon-shaped piece of lead foil held in place with adhesive strips. 3. They can be arranged in parallel rows, unless the center two-thirds or active portion of the needle does not extend 2 to 3 cm. beyond the border of the tumor. In such instances, another insertion is made at right angles to the border of the lesion, closing one or

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Read in the Symposium on Cutaneous Malignancy, an Appropriate Segment of Dermatology, before the Section on Dermatology and Syphilology at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

1. Lehmann, C. F., and Pipkin, J. L.: Interstitial Radium Therapy: Description of a Short Intensive Technic, A. M. A. Arch. Dermat. & Syph. **63**: 312-322 (March) 1951.

both ends as the need arises. 4. Another possibility is a rectangular or hexagonal arrangement. If more than four needles are thus arranged, the needles are placed in the center of the lesion 5 mm. apart. Their distribution varies with the intensity desired. We have learned that, if we want an intensive dose, we should place the needle

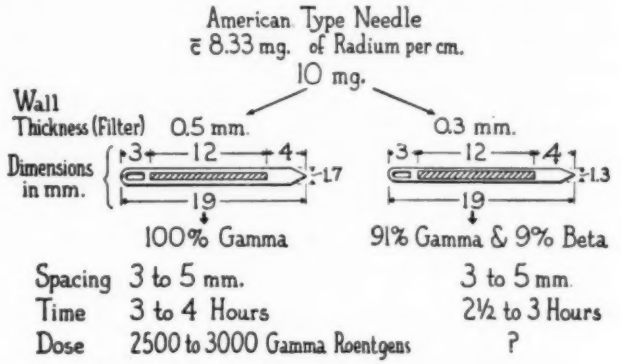

Fig. 1.—Diagram of short-time high-intensity technique of radium therapy of malignant cutaneous disease.

walls as close as 3 mm. apart (4.3 mm. between the needle axes).

In most skin cancers arrangement of the needles in one plane in the base of the lesion is sufficient. If the carcinoma is projecting more than 0.5 cm. above the skin level, it may be trimmed down by the knife or endotherm cutting current, so that it is only necessary to treat with needles in one plane. After the needles are placed, a strip of adhesive tape is put over the lesion so that it fixes the end of them. This is sufficient to hold them in place.

No shielding is used except near the eye or on the lip. A strip of lead is placed on top of the lesion if necessary to prevent a reaction on an opposed surface; for instance, if the needles are placed on the lower lip, the lesion is covered with lead to prevent a reaction on the upper lip. Lead foil 3 mm. thick is used to cover the area that is being treated.

This short intensive technique uses beta and gamma rays of radium. The rays emitted through 0.3 mm. of platinum are 91% gamma and 9% beta.[2] Needles with filtration of 0.3 mm. of platinum are left in place for 2½ to 3 hours. If all beta rays of a 10-mg. needle are filtered out by the use of 0.5 mm. of platinum, the treatment time would have to be extended to 3½ to 4½ hours, depending on the total amount of radium used (fig. 2). We do this occasionally, and include it under the short-time technique.

ADVANTAGES OF THE SHORT INTENSIVE TECHNIQUE

The short intensive method has certain advantages in the treatment of small or early skin cancers. 1. It can be an office procedure and does not necessitate hospitalization, thus saving hospital beds and money to the patient. 2. Being given in a single treatment, it saves the patient repeated trips, which are usually necessary in administering other forms of radiation given in a fractionated, protracted series of treatments. This is a distinct advantage to patients who have to travel distances to a treatment center and in treating the aged or crippled (who have difficulty in getting to a physician). 3. Because of the short treatment time, it is an economical use of radium. This is of advantage in clinics where there may be a waiting list for radium. 4. Because of the short length of the needles, it affords a method of treating lesions in certain locations where shielding is difficult or when an intensive dosage of radiation is desired in a small area.

LOCATIONS OF SUITABLE LESIONS

Lesions in Eyelids and Canthi.—Small lesions on the eyelids, even those on the edge of an eyelid, are suitable for treatment. To protect the eye and to confine the reaction of the radium to a very small area, strips of lead foil (3 mm. thick) are placed under the projecting ends of the needles and on the surface of the lesion. A gold-plated eye shield is also placed in the conjunctival sac. This method of shielding filters all beta rays, and the gamma ray dosage passing through is not of sufficient intensity to cause even an erythema.

Lesions on the eyelids respond as well as lesions in the canthus. It is again emphasized that this technique is applicable only to the smaller, more superficial cancers. Infiltrating lesions in the inner canthus that extend along the orbital wall are not treated with the short intensive method.

Lesions in Sulci.—This technique is very suitable for treatment at the nasolabial and posterior auricular folds, where shielding for x-ray treatment is more difficult and more than one plane in the field is essential. This short intensive technique has been used advantageously in treatment of basal cell carcinoma in the concha or outer auricular canal.

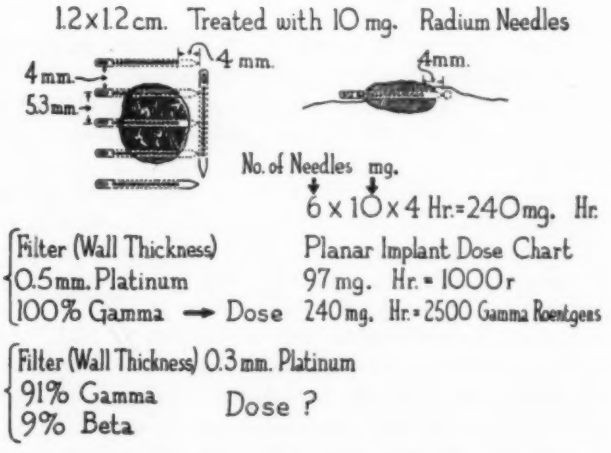

Fig. 2.—Example of use of short intensive technique in treatment of a squamous cell carcinoma.

Lesions on Auricles.—Cancers on the external ear offer a problem at times when the cosmetic result is considered. The lesions that have not invaded cartilage are amenable to this technique in a high percentage of instances.

2. Stenstrom, W.; Quimby, E. H., and Pendergrass, E. P.: Report of the Research and Standardization Committee of the American Radium Society, Am. J. Roentgenol. **43**: 118-125 (Jan.) 1940.

LONG-TIME LOW-INTENSITY TECHNIQUE

The long-time low-intensity technique has evolved over the past 25 years and has been used by numerous workers. It has been popularized by Cade in England and numerous others in America.[3] It makes use of needles containing small amounts of radium that are left

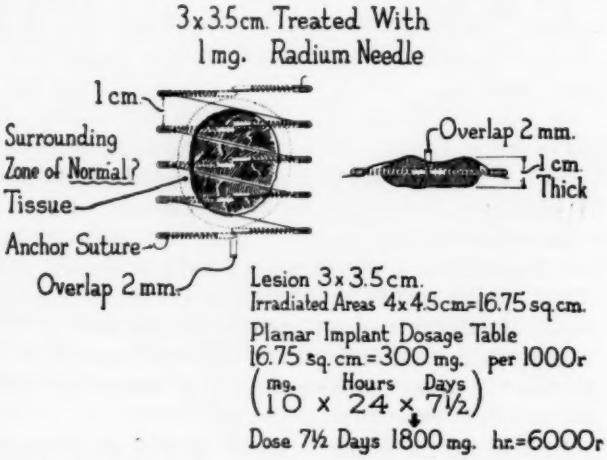

Fig. 3.—Diagram of use of the long-time low-intensity technique in treatment of basosquamous cell carcinoma.

in place a long time (7 to 10 days). The strength of the needles averages about 0.66 mg. per centimeter, and the thickness of their walls varies from 0.5 to 0.8 mm. of platinum. A shield of 0.5 mm. of platinum filters out 99% of the beta rays and 0.8 mm. filters out all but the harder gamma rays. It has been found that this technique of gamma ray radiation and the time-dosage relationship of one week's radiation with such needles produces as selective an effect as possible, i. e., a cancerocidal dose that produces a minimal amount of radiation damage to normal tissue.

This technique is selected for treatment of deeply infiltrating lesions or extensive lesions that vary from 3 to 5 cm. in their longest diameter. (Lesions that cover a larger area can be more expeditiously treated with x-rays.)

It is also used for treatment of lesions with highly differentiated cells in locations where lesions notably are resistant. Experience has taught that skin cancers in certain locations are resistant. The explanation is not always due to the grade of the cancer cell but to other factors, too. One of these may be the "cancer-bed," as it is known that as good a selective effect cannot be secured in a cancer in a poorly vascularized bed as in one in a bed that has abundant vessels. For instance, most lip cancers are well differentiated and, based on the "grading" factors, should be highly resistant. Yet almost all of the smaller ones respond satisfactorily to the "short-time" technique. On the contrary, cancers on the sides and back of the neck (whether basal cell, basosquamous, or squamous cell) are more resistant than lip cancers. It is on the extremities, particularly on the back of the hand, that the "cancer-bed" influence is seen. It is here particularly that the selective effect of the long-time low-intensity technique is best illustrated. If one treats this with soft rays, the scar is less supple and is apt to break down easier and does not withstand physical trauma as well as the scar resulting from treatment with gamma radiation (the long-time low-intensity method). In figure 3 the long-time low-intensity technique in a basosquamous (or squamous cell) carcinoma is outlined.

TECHNIQUE

The needles that we have used for this technique contain approximately 0.66 mg. of radium per centimeter. Their wall thickness (filtration) is 0.5 mm. of platinum and their over-all length is 27.7 cm. (fig. 4). They are placed in tissue 1 cm. apart. The ones on the outside of a lesion are placed at the border of the palpable growth (so as to radiate well beyond the cancer). If the ends of the active portion of the needle do not include the palpable induration, one or more are inserted at right angles so that a proper dosage is distributed throughout all of the cancer. They are placed in the vast majority of instances in a single plane at the base of the lesion. Most skin cancers treated with radium by us are not thicker than 1 cm. and do not call for more than a one-plane insertion. The needles are inserted so that their eyes are out of tissue, and they are placed either in the base or in the borders where there is enough tough stroma to support them. They are then fixed in place by suturing.

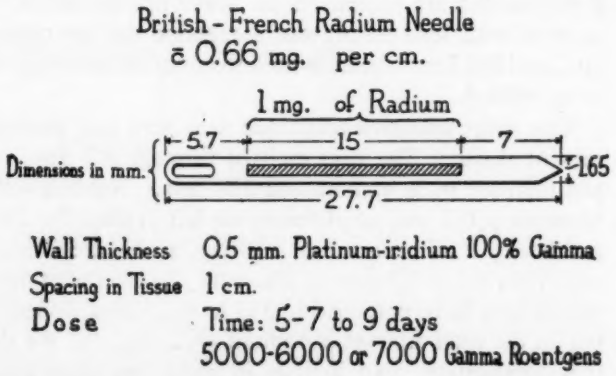

Fig. 4.—Diagram of needle used in long-time low-intensity technique of radium treatment.

Various methods of suturing may be devised; each needle may be anchored individually, or the sutures may be criss-crossed over the top of the growth by insertion of the needles alternately in opposite directions. Thus a mattress of sutures and needles is formed, and anchoring sutures are used at various places where there is normal firm skin to hold. Usually fine wire suturing material is used.

3. Cade, S.: Malignant Disease and Its Treatment by Radium, ed. 2, Baltimore, Williams & Wilkins Company, 1948, vol. 1, p. 43. Martin, C. L.: Small Radium Needles Versus Radon Implants, Am. J. Roentgenol. **27**: 240-248 (Feb.) 1932. Martin, C. L.: Weak Radium Needle Technique in Carcinoma of Cheek, ibid. **43**: 226-236 (Feb.) 1940. Martin, C. L.: Layer Technique in Radium Needle Therapy, ibid. **48**: 377-383 (Sept.) 1942. Martin, C. L., and Martin, J. A.: Treatment of Advanced Cancer Involving the Ear, ibid. **60**: 750-757 (Dec.) 1948. Cole, H. N., and Driver, J. R.: Radium Dosage and Technique in Carcinoma of Skin, with Special Reference to Interstitial Irradiation with Platinum Iridium Needles, ibid. **33**: 682-689 (May) 1935. Shelmire, B., and Fox, E. C.: Small Radium Needles in Treatment of Malignant Cutaneous Tumors, Arch. Dermat. & Syph. **34**: 862-872 (Nov.) 1936. Lamb, J. H., and Eastland, W. E.: Cancer of Lower Lip: Treatment with Radiation, J. A. M. A. **117**: 600-607 (Aug. 23) 1941. Howell, J. B.: Cancer of the Center Face, South. M. J. **43**: 283-291 (April) 1950.

The dosage given to skin carcinomas by this technique varies from 4,000 to 6,000 γ r. In calculating doses in gamma roentgens, one can use tables devised by Paterson and Parker, one that is readily available being in the book "Physical Foundations of Radiology."[4]

When the interstitial application of radium is selected as the method of choice for the malignant cutaneous condition at hand, a decision must be made as to which of these techniques is most suitable. The size, the shape, the depth, the location, the type, and the grade of the neoplasm influence the selection. The tumor bed and the adjacent structures also influence this. Previous treatment, scar tissue in or around the new growth, the presence of other disease processes adjacent to the neoplasm, and the proximity to vulnerable structures as well as the physical aspects of the tumor and the surrounding tissue all influence the choice. The patient's age, physical and mental condition, and ability to travel also determine which technique is used.

AREA TREATED

In treatment of a malignant lesion by radiation, the question always arises as to how large an area is to be treated. As a rule the larger the lesion (in area) the wider the border around it is radiated. A border varying in width from one-third to one-fourth the largest diameter of the lesion is usually treated, the maximum border usually being not over 0.5 cm. and the minimum not less than 3 mm. All of the macroscopically abnormal skin around the lesion is treated, such as borders showing hyperkeratosis or telangiectasia.

In producing anesthesia, 2% procaine hydrochloride is used as an anesthetic in the Cook's dental syringe with a 1 or 1½ in. (2.5 to 3.8 cm.) gage needle. This facilitates the infiltration of the anesthetic with very little pain and trauma. A small wheal is first made by intradermal injection 0.75 cm. outside of the surface outline of the tumor, and the long needle is thrust through the supposedly normal tissue, outside and parallel to the surface outline of the new growth. It is better to infiltrate around and under the tumor rather than into it, as this distention distorts the tumor; after the anesthetic is absorbed, the needles will lie closer together than when initially implanted.

At times cancerous tissue lying below the surface outline will be defined by the infiltration. The soft cancerous tissue will give way to the solution to leak into the tumor or the solution to distention of the tumor, visible leakage into the sudden release of resistance on the needle indicates that the point of the needle is in the growth; therefore the skin surface outline should be marked at this point. By replacement of the needle laterally and reinjection of the solution, the true confines of the tumor can be ferreted out. This technique has been very valuable to us in establishing the actual boundaries of the "iceberg type" of infiltrating carcinoma.

The infiltration of the normal skin with the anesthetic around the tumor elevates a peripheral plateau, making insertion of the needles horizontal to the skin and to the base of the tumor an easy procedure. Without this surrounding elevated plateau and a ballooning up of the tumor, it is difficult in some sites to introduce the needle from a flat surface through a small skin puncture so that it lies at a depth of 0.5 cm. parallel to the surface and the tumor base. If the tumor is of the exophytic type and more than 1 or 1.5 cm. thick, it may be reduced by electrosurgery to the proper thickness for a single row of radium needles placed parallel and horizontal to the surface and the tumor base.

RADIONECROSIS

The primary object of radiation therapy (whether by x-rays or radium) is to kill all of the cancer cells. To do this in using radium, one must arrange the needles so that the minimal dose in any part of the lesion is cancerocidal. There are certain rules to follow that give fair assurance of this result. However, experience also teaches this, and one's technique improves with practice. If the physician is overzealous in dosage, he is apt to have more radionecrosis of tissue than he should, and he defeats the second object of radiation therapy. This is to get as selective an effect as possible.

Radionecrosis may appear early or late. An ulceration after the cancer sloughs away that does not heal in a few weeks (five to six) is due to overdosage, and the radiation treatment in such an instance is no less than actual cauterization. In such an event, the effect from electrocoagulation or actual cautery is better.

Early radionecrosis is more of a hazard with beta radiation than with gamma radiation. If it occurs, it is usually due to placement of the needles too close together, or leaving them in place too long. Late radionecrosis may occur following use of any method. It usually is seen in areas where there is scanty blood supply, however, such as on the back of the hand, or after treatment of a cancer in scar tissue. In such an event, the scar needs to be excised and a skin graft made.

Frequently one can anticipate late radionecrosis, and in such an event should so advise the patient. In such a case the question naturally would be advanced: why use radium at all, and not go ahead with extensive surgery and plastic repair? This is logical. However, it is our opinion that if radiation therapy is used for cancer destruction, it is best to use it preoperatively rather than postoperatively. When used thusly, it frequently reduces the extent of surgery, which is of particular advantage when a cosmetic question is raised, as it sterilizes the surrounding field of cancer cells.

SELECTION OF TECHNIQUES

To avoid radionecrosis as much as possible the short intensive method is used on the smaller carcinomas, usually those less than 1 cm. in diameter and not over 0.5 cm. in depth. There is a limit in the amount of short intensive radiation that should be given to normal structures, and we rarely use over 5 10-mg. needles for this beta radiation. If a larger area is to be treated, it is best to use gamma radiation with the long-time low-intensity technique.

In regard to radium versus x-rays, we hold no particular brief for radium. We freely admit that equally

4. Glasser, O.; Quimby, E. H.; Taylor, L. S., and Weatherwax, J. L.: Physical Foundations of Radiology, New York, Paul B. Hoeber, Inc. 1947, p. 310.

good results can be obtained with x-rays when the proper technique is selected for the individual case. It is our feeling that there is less chance of missing cancer cells around the borders in using radium interstitially than in treating with x-rays. We select radium in most of our cases because of the saving to patients in time and number of visits.

EXPENSE OF RADIUM SERVICE IN AN OFFICE

One question that is frequently asked about instituting radium therapy is what the expense would be. This item is not prohibitive. For an average dermatological practice, one can take care of most malignant skin lesions with 6 10-mg. needles (a total of 60 mg.) and 6 1-mg. needles (a total of 6 mg.)—the cost of which would be well below the cost of an x-ray machine.

The cost of maintaining a radium-treatment service lies not so much in the cost of radium as in the cost of office space devoted to it. One should have a suitable "parking" room with properly leaded walls in which to place patients treated with radium, and these rooms should be as far from the main activities of the office as possible so as to get the advantage of distance in protection of office personnel from stray radiation. Other precautions include properly leaded storage containers for the radium. These and also all other precautions necessary for protection of the operator and technicians from excessive radiation are important factors to consider if a dermatologist institutes radium therapy in his armamentarium against skin cancer.

RESULTS

The end-result of radium therapy to carcinoma of the skin is quite satisfactory. We have been using radium interstitially for 30 years and the long-time low-intensity technique for 19 years. Over these periods 8,892 skin cancers have been treated. A statistical survey based on five year cures in this series of cases was unsatisfactory owing to the following factors: (1) the high death rate in the elderly from intercurrent diseases during any five year period; (2) difficulty of a routine follow-up in the elderly; (3) the fact that some 3,000 of these lesions were treated less than five years ago and that sufficient time has not elapsed to include them in a series of five year cures; (4) lack of knowledge of histological diagnosis in all treated cases; and (5) change in the material in the last half of our experience so that the first half is not comparable. During the past 10 years the lesions were seen earlier and therefore were smaller and easier to handle. This is probably due to the educational campaign fostered by the American Cancer Society. There were fewer complications from maltreatment, and the lesions were more critically selected for radiation therapy during the last half of this period. Therefore, the following remarks must be considered as a personal interpretation of experience and not a scientific assessment based on accurate statistical data accumulated over this entire period.

In spite of the above objections, the end results are certain in a great number of these patients, as follow-up observations were requested five to six weeks after treatment, twice more at two month intervals, and then yearly. Many patients were observed months or years later and the result noted when they were seen for some other dermatoses or subsequent tumor. Spot-checking groups of consecutive cases for a given period of time reflects results and indicates certain trends from which definite conclusions can be drawn.

Cure Rate and the End-Result.—The cure rate and the end-result in regard to a serviceable scar obtained by a particular method of irradiation are influenced by the size, depth, location, and cell character of the lesion as well as the previous treatment, the cancer bed, the presence or absence of infection, and the age of the patient. These factors constitute the premise for the assignment of a particular method for the problem at hand; therefore they must be considered in assessing results.

In 1935 we estimated rate of cure from the long-time low-intensity method (which is used on the large radioresistant or previously treated lesions) at 80%; and the rate of cure from the short intensive method (which is used on the small superficial selected lesions) at 95%. In 1945 the cure rate with the first technique was 95%, and with the second method it was 97%.

A more critical analysis of our statistics gave us the following rates: The absolute cure rate (which is based upon all lesions, including untreated as well as treated) was 60% for the first five years of this series. In 1945, this had increased to 85%. This was not due to an improvement of technique, but to the fact that fewer advanced hopeless cancers were seen. The relative cure rate of all cases (which is based only on treated cases) was 90%. The net cure rate (which is based on treated patients after elimination of those dying of intercurrent diseases and those lost to observation) was 95%.

714 Medical Arts Bldg.

Malnutrition in Old Age.—Malnutrition is a . . . serious problem in old age. Only 20% of the men and women in my series over the age of 61 were moderately overweight, and only 10% could be called obese, whereas 30% of the men and 20% of the women were definitely under normal weight. Nutrition is easily assailed by many chronic infections and diseases that impose inactivity. The amount of weight lost by an edematous cardiac patient is surprising when compensation is restored. The demineralization of bones in plaster casts and on rest in bed is recognized; osteomalacia and osteoporosis are fairly common. But there are other enemies too, such as the absence of teeth and the presence of diseased or poorly placed teeth. Appetite changes when a job, with its regular hours and discipline, is gone. Sadness makes one person a skeleton and another a glutton. People who enter homes for the aged or public almshouses and eat with others who are like what they will soon become, have little zest in eating; so do those who have to eat alone, at home or in unfriendly restaurants. Alcoholism is resorted to by some aging people as a release from sorrow or loss of job. Food fads and fears find an eager audience in old people. Therefore, the prescription of a normal diet is proper, but it does not go far enough. Vitamin supplements are attractive. The really important therapy of malnutrition is unorthodox. It is independence, exercise, occupation, friends to eat with, a good place to live in and good care of disabilities.—R. T. Monroe, M.D., The Effect of Aging of Population on General Health Problems, *The New England Journal of Medicine*, Aug. 20, 1953.

DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE EYELIDS

Eugene F. Traub, M.D., New York

Cutaneous cancer accounts for from 40 to 60% of all types of malignant lesions seen by the family physician. Carcinoma of the eyelid occurs in the older age group primarily; three-quarters of the patients are past 50 years of age. Men are slightly more susceptible to carcinoma of the eyelid than women; this is particularly true of the clinic groups. Of the facial epitheliomas, approximately 10 to 15% occurred about the eyelids,[1] although extremes of 2.73 to 55% were noted in various reported studies. According to Hasley,[2] 15% of all tumors of the lid are malignant. In all recorded series,[3] the greatest number of eyelid lesions were found on the inner canthus (table 1). The lower lid was also a common site for the development of lesions, particularly on its medial portion in the area toward the inner canthus. Four-fifths of all lower lid lesions were found there. Consequently, then, cancer of the eyelid is not an infrequent occurrence, but what makes it still more significant is the fact that more than one-third of the cases fail to be cured by primary surgery, irradiation, or both. In a fair percentage of cases, loss of sight occurred on the side of the affected eye. Enucleation because of invasion of the orbit was required in 4 of 82 of Robinson's [3] cases. This is largely due to the fact that, in advancing lesions, long slender strands of tumor cells emanate multicentrically through the lymphatics from the body of the lesion, "iceberging," for some distance to form what appear to be multiple foci of origin. This histological feature explains the persistent recurrence of tumors in this area after apparently thorough extirpation. It also makes therapeutic approach to lid lesions more difficult, because it requires more skill to effect a cure and it makes cure especially necessary in the initial treatment. At the same time, preservation of tissue and function is all important. The method of treatment for each case must, to a certain degree, be individualized to best protect the lens, cornea, lacrimal duct, and tarsal plate and to maintain lid margins and eyelashes.

ETIOLOGY

Irritation is an important factor to associate with the majority of cancers of the eyelids. Ill-fitting, irritating eyeglasses, especially those in which the nose piece is worn or rough, burns caused by the sun at the edge of rimless glasses, scars from burns of any origin (gasoline, ether, or hot grease), scars and irritation from repeated styes, coal tar derivatives (oil and petroleum) accidentally rubbed on the eyelids by mechanics and garage workers are all possible sources. Single injuries from shell fragments have been followed three years later by a basal cell epithelioma according to Marconcini.[4]

PATHOLOGY

With most cancers about the lids it is difficult to determine the exact site of origin, but frequently the mucocutaneous junction is involved. Most of the cases in my series apparently arose on the skin surface near the eyelid margin and then extended to the mucocutaneous junction early in development. This was also the experience of Martin.[5] In a number of patients, the growth appeared to have originated in or near the opening of the lacrimal duct. Basal cell epitheliomas may also arise from Meibomian sebaceous glands and more rarely from the glands of Zeis along the hair follicles according to Morax.[6] Small cystic adenomas along the outer aspects of the eyelids are considered to arise from the sweat glands of Moll. The squamous cell cancer may begin as a hypertrophic warty growth or a hyperkeratosis, which, after thickening, develops central necrosis, or as in this series it may arise from normal skin. In contrast to the basal cell epithelioma, this lesion develops rapidly. It is more apt to invade and destroy tissue, and, while it is capable of metastasizing to the regional lymph nodes, such a course is apparently not an early manifestation in lesions about the eyelid any more than it is in other early squamous cell lesions of the glabrous skin. Preauricular or upper deep cervical lymph nodes are first affected when metastasis does occur.

Although constituting a single histological and nosological species, the development of the basocellular epithelioma tends to take an extremely variable course so that it may present itself clinically in highly varied forms, such as nodules surrounding a cicatrix, an eroded surface, an ulcer with rolled pearly bordered edge, a pigmented or plain tumor, a cystic type lesion, a morphea-like plaque, or an invasive or fungating growth. Moreover, the types may coexist or follow one another. Even a squamous cell growth may develop in some portion of the tumor. Characteristically, the basal cell tumors grow extremely slowly and usually take months or years in their development. The invasive type, which extends downward and inward and readily invades bone or cartilage, grows somewhat more rapidly than most of the other basocellular varieties. In general it has been observed that the deeper the ulceration, the greater the degree of malignancy.

The so-called rodent ulcer, with either nodules or pigment, is the commonest of the group seen on the eyelids. It usually begins as a small firm nodule with a smooth shiny surface. At this stage it may resemble the intradermal nevus or "common mole" not infrequently seen on the lid margin. While the tumor slowly enlarges

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Because of lack of space, some of the tables have been omitted from THE JOURNAL and will appear in the author's reprints.

Read in the Symposium on Cutaneous Malignancy, an Appropriate Segment of Dermatology, before the Section on Dermatology and Syphilology at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

1. Eller, J. J., and Eller, W. D.: Tumors of the Skin: Benign and Malignant, ed. 2, Philadelphia, Lea & Febiger, 1951, pp. 399-404.

2. Hasley, C. K.: Roentgenologic and Dermatologic Aspects of Tumors of Eyelid, Society Transactions, Arch. Ophth. **25**: 926-927 (May) 1941.

3. Robinson, G. A.: Cancer of Eyelids, Am. J. Roentgenol. **38**: 743-745, 1937.

4. Marconcini, E.: Basal Cell Epithelioma of Eyelid Probably of Traumatic Origin, Arch. ottal. **55**: 623-631, 1951.

5. Martin, H. E.: Cancer of Eyelids, Arch. Ophth. **22**: 1-20 (July) 1939.

6. Morax, V.: Cancer de l'appareil visuel, Paris, Gaston Doin & Cie, 1926, pp. 1-136.

peripherally, there is a tendency for more rapid downward extension, particularly beneath the ulcerated portion. As further infiltration takes place, contracture of the lid, with resulting ectropion, may take place. Pigment may be a marked feature of some of these tumors causing them to resemble melanomas. In the invasive type of basal cell lesion, growth may extend deep into the orbital cavity and may eventually erode the skull bones. If located at the inner canthus, penetration of the thin osseous layer bounding the nasal cavity may occur and involve the internal structures of the nose. Rarely the tarsal conjunctiva is the site of origin of a carcinoma; in this case extension usually occurs over the rest of the conjunctiva and the tarsus is seldom penetrated or the skin involved. Squamous cell lesions, however, have a greater tendency to invade the tarsal cartilage.

DIFFERENTIAL DIAGNOSIS

Malignant lesions on or about the lids are most frequently confused with the "common mole" or intradermal nevus or the "warty" or verrucous lesions, especially of the seborrheic type. Chalazion may be mistaken for an adenocarcinoma of the Meibomian glands; hidrocystoma has, on several occasions, been mistaken for a malignant melanoma. The cystic type of basal cell epitheliomas has been thought to be a benign cyst, while the larger lesions seen in multiple benign cystic epithelioma often need microscopic differentiation. The ordinary stye or small furuncle in no way resembles a basal cell epithelioma, but the acutely inflamed and rapidly developing early squamous cell epithelioma does resemble and may often be confused with a simple pyogenic lesion. Irritated verrucous lesions must be carefully differentiated from squamous cell epithelioma. Xanthelasma is so distinctive that it offers no problem.

TREATMENT

There seems to be general agreement among all cancer specialists, including surgeons, that surgery should be avoided if possible in dealing with carcinoma of the lids. Even the removal of a small basal cell epithelioma of the lid margin would require hospitalization for surgical care and would generally involve more or less complicated plastic repair. The results obtained by even the most qualified surgeons, while they might compare favorably from the standpoint of percentage of cure, fall far short of the cosmetic appearance that may be achieved by other methods without either hospitalization or great discomfort to the patient.

For these reasons, I wish to emphasize methods other than surgery. Most of these demand irradiation of some type. The combination method is vastly superior to all others, on the basis of the results obtained by most workers. This method has the advantage of simplicity and efficiency and lacks most of the danger that might follow massive doses of radiation. It has still another very important feature, and that is that all finger-like extensions of the growth ("iceberging") are discovered at once and the field of subsequent radiation may then be absolutely and accurately delineated.

An excess of procaine (Novocaine) hydrochloride is intentionally injected directly under the lesion to lift it up and away from underlying structures. Biopsy is made at this time by simple scalpel excision. A pathological record is well worth while, even though most lesions can readily be identified clinically. Desiccation is used solely to minimize bleeding and to make follow-up curettement easier. Thorough curettement of the base and margins of the lesion is the most important part of the entire procedure. With experience, it is easy to know exactly when the entire field has been curetted free of tumor tissue; the new growth is always friable and scrapes away readily, whereas the normal tissue cells are tough and cause the curet to slip over them. The curet may be thrust into all small finger-like pockets, and once discovered they can be thoroughly cleaned out. Desiccation alone, lacking any sense of touch, never gives one this feeling of assurance. Once the boundaries of the lesion have been found, the exact field to be irradiated can easily be mapped. I believe that the occasional radiation failures occur because a field large enough to cover all such finger-like processes of the growth has not been used. Such radiation failure could, of course, be corrected by subsequent radiation treatment, but this causes greater tissue damage and is practically never necessary when the combination method is used.

The final step is irradiation of the open wound. This is usually done immediately after removal of diseased tissue. If there is excessive bleeding— there is seldom much, but sometimes oozing of blood does occur—the base of the wound may be superficially desiccated to stop it. Healing takes place more promptly, if this latter step can be omitted. The dosage of radiation required is the minimum one necessary to kill the few remaining cancer cells since no thickness of tumor remains to be penetrated. Either roentgen rays or radium may be used. Assuming the curettement has been ably accomplished, a dosage of 1,500 to 2,500 r, given with low voltage (100 kv.) unfiltered x-rays, is almost invariably sufficient. This is a one dosage, one treatment procedure. Provided the growth is an early one that has not been previously treated or neglected, this method should accomplish better than 95% cure with one treatment. Radium in equivalent dosage may be employed either interstitially or by surface application; however, when it is possible to completely remove the tumor, surface application generally suffices.

Probably a majority of dermatologists and radiotherapeutists use radiation therapy alone, and each one develops a more or less individual technique. Because of the excellent results achieved, I believe that several of these methods should be outlined. Ward,[7] using a high voltage load and almost uniformly 1 mm. aluminum filter, gave doses generally of either 3,000 or 5,000 r divided into 4 or 10 rather closely grouped treatment dates. His fields varied from approximately 2 to 7 square centimeters. His results were excellent not only because of the percentage of cures but also because of the fine cosmetic and functional results achieved. His lowest total dosage was 1,800 r. Others have used similar total dosage but with low voltage, unfiltered divided radiation.

Contact roentgen therapy, with its tremendous output and low depth dose together with the short exposure time,

7. Ward, W. H.: Problem of Skin Cancer, Australian J. Dermat. 1: 157, 1952.

may prove valuable in treating eyelid lesions, but special equipment and techniques are necessary. According to Andrews,[8] the results of the treatments of epitheliomas with a Phillips tube are no better than, and even not so good as, those obtained with standard superficial therapy machines and unfiltered radiation produced by 60 to 100 kv. The end of the tube is of a size that an epithelioma only 1 cm. in diameter can be adequately exposed. The advantage is the small depth dose, less than 1 cm., makes it a suitable treatment vehicle for cancer of the eyelids. The policy of giving large doses of this type of radiation within a few seconds is a great advantage because the patient cannot hold the lid still for long. Grenz rays may be used, and though Eller [1] illustrates a 10 year cure he does not recommend the method in his textbook.

Radium treatment for lid lesions also has many exponents, and again procedures vary greatly not only in use of interstitial radiation instead of surface applications or employment of radon but in the exact methods of application of each. At first 5, 10, or even 20 mg. needles were employed for a relatively short period of time. More recently, Howell [9] and others found that far more excellent cosmetic and functional results were achieved using 1 to 2 mg. needles left in place for long periods (five to seven days).

According to Howell,[9] the use of low voltage x-ray therapy for superficial lesions of small size involving the central portion of the lower lid is an excellent procedure and is considered the treatment of choice by many. For infiltrating lesions of the canthi and lids, x-ray therapy is inferior to low intensity radium needle therapy. X-ray therapy frequently is followed by recurrences, and the depth dose received is often inadequate for lesions situated in the region of the inner canthus. It is in this situation that treatment with the low intensity radium needle has proved most valuable (table 2 and 3).

COMPLICATIONS OF RADIATION THERAPY

Because irradiation, employed either alone or as part of a combination treatment, seems to be the treatment of choice for the vast majority of cases of cancer of the eyelids, the dangers inherent in this remedy should be thoroughly understood. Effects of irradiation on the eye conjunctiva precedes the skin response by three to five days. The cornea shows remarkably little reaction to irradiation, but Martin [10] has described a loss of luster through the cornea with diminution in sensation followed rarely by ulceration three months after intensive radiation therapy. Glaucoma has been reported by Peter [11] after irradiation, but this must be an extremely rare complication as it is not generally reported. The iris, retina, and aqueous and vitreous humors do not appear susceptible to irradiation. The crystalline lens is very susceptible to injury by irradiation, although a period of 3 to 12 months may elapse before cataract becomes apparent. Cataracts following irradiation have been reported.[12]

The rapidity of onset and degree of opacity of irradiation cataracts depend on the dosage delivered to the lens and on the age and general susceptibility of the patient's eye to this type of insult. Cataracts produced by roentgen rays and radium appear similar to those resulting from infrared and ultraviolet light, and it is probable that latent injury produced by one agent would be added to that produced by the others. Lenses suffering from incipient cataract owing to senility or other cause would be more susceptible to progressive cataract than a normal lens. Many instances of neurodermatitis, atopic eczema, or congenital ectodermal dysplasia, accompanied with asthma, have been complicated by juvenile cataracts.

The threshold dosage productive of irradiation cataract does not appear to have been established according to the literature, although Kumer and Sallmann [13] warn against the delivery of more than an erythema dose of roentgen rays or radium to the eyeball. Cataracts may appear from six months to eight or more years after irradiation. It is also apparent that in many instances in

TABLE 2.—*Summary of Author's Cases*

No. of patients	33	
No. of lesions	50	36 on eyelids
Patients with lesions on both eyelids	3	
Combination treatment	28	Fulguration, curettement, and either x-ray or radium
Radium only	1	
X-rays only	0	
Electrodesiccation and curettement only	3	
Sherwell cautery	4	
No. cured in one treatment	31	
No. receiving 2 treatments	4	
No. requiring 3 or more treatments	1	
No. of cases previously treated.	10	Lesion burned off 10 and again 3 or 4 yr. before (1 treatment)
		Two basal cell epitheliomas received many radium treatments over a period of 7 yr. (1 treatment)
		Patient received innumerable treatments with x-rays, radium, and desiccation over a 10 yr. period; received 2 treatments; and recently returned again with recurrence
		Five previous x-ray treatments with recurrences (1 treatment)
		Duration 6 yr.; lesion had been removed 5 yr. before but had recurred (1 treatment)
		Deep x-ray treatments followed by injections of penicillin (1 treatment)
		Previous electric needle treatment (2 treatments)
		15 x-ray treatments without cure (3 treatments)
		Lesion treated 4 yr. earlier with x-rays and 3 yr. earlier with electric needle (2 treatments)
		Two previous unsuccessful removals (1 treatment)
Duration of apparent cure		
1-3 yr	23	
3-5 yr	4	
Over 5 yr	9	
Lesions for which follow-up plastic surgery was desirable.	1	
No. of squamous cell epitheliomas	5	
No. of treatments to effect cure of squamous cell epithelioma.	1	

8. Andrews, G. C.: Precancerous and Cancerous Dermatoses of Skin, New York J. Med. **50**: 1655, 1950.

9. Howell, J. B.: Cancer of Center Face, South. M. J. **43**: 283-291, 1950.

10. Martin, P.: Effect on Eye of Radium Used for Treatment of Malignant Disease in Neighbourhood (Hunterian Lecture), Brit. M. J. **1**: 651-654, 1937.

11. Peter, G.: X-Rays and Radium in Treatment of Tumors of Conjunctiva, Radiology **25**: 745-749, 1935.

12. Hunt, H. B.: Cancer of Eyelid Treated by Radiation, with Consideration of Irradiation Cataract, Am. J. Roentgenol. **57**: 160-180, 1947.

13. Kumer, L., and Sallmann, L.: Die Radiumbehandlung in der Augenheilkunde, Wien, Springer-Verlag, 1939.

which cataracts developed this might well have been avoided by using proper eye shields, directing the rays at angles that would avoid placing the lens in the direct target range, or by employing other methods in cases in which this could not be done. Roentgen therapy, when applied with proper shielding of the eyeball, carries definitely less hazard of irradiation cataract than does radium therapy since the eyeball and lens can be effectively protected against superficial roentgen rays and beta rays with a shield equivalent to 1 mm. of lead. No eye shield is adequate for protection against the more penetrating gamma rays. The ophthalmoscopic [12] appearance of early irradiation cataract presents rather typical features and may be identified as such, but, when these changes progress to total cataract of the lens, it then loses these characteristics.

COMMENT

Early diagnosis, together with prompt adequate therapy, is needed more in lesions of the eyelids than in any other field of cancer because a good cosmetic result, as well as a functional one, is of prime importance. Since most basal cell epitheliomas apparently arise on the skin surface near the lid margin and gradually spread to invade the canthi, mucocutaneous margin, and finally the deeper structures, it is obvious that the cure rate is highest the earlier the treatment is given. Except for those in 10 previously treated patients in my series (table 1), all were early lesions that should have been cured in one treatment. Since it is felt that eyelid lesions should be followed at least three years before cure is certain, 23 of the 36 lesions in this series are listed as apparent cures even though many of them had been observed over two years. Of the 36 lesions, 31 were apparently cured in one treatment. Of the 10 previously treated patients, 6 received one treatment, 2 required two treatments, and 2 (both having had many previous x-ray and other types of therapy) were given three or more treatments. The five cases of squamous cell epitheliomas were recognized early, received slightly more irradiation than the basal cell epitheliomas, and were all apparently cured in one treatment. Three had more than the required three year observation period and can be considered cured. As noted in other series, many of the patients presented basal cell epitheliomas or keratoses elsewhere than on the eyelids. Driver and Cole [14] report this in 47% of their cases, Sharp [15] in 33%, and Hunt [12] in 28%. Several of the group had cancers simultaneously on both lids. Progression from one inner canthus to the opposite one has been noted repeatedly by myself and others.

In a fair percentage of cases in the literature, the lesions were advanced cancers requiring enucleation for invasion of the orbit. Others must have been late squamous cell epitheliomas that had metastasized. None of the squamous cell epitheliomas of the face that I have seen [16] have had node involvement before four to six months, but others state that metastasis may occur early. There were no mixed or transitional epitheliomas in this series, Welton and co-workers [17] reported 97.1% five year cures in 1,052 patients with cutaneous cancer treated by use of curettage, electrothermic, and roentgen ray therapy. There seems to be every reason to believe that this method is the treatment of choice for cancer of the eyelids as well. Four previously irradiated lesions were treated satisfactorily by the chemocautery of Sherwell preceded by curettement. This method is not recommended, however, because it is almost impossible to protect surrounding tissues against the destructive effects of the chemical.

SUMMARY AND CONCLUSIONS

The various types of cutaneous malignancies found on and about the eyelids are enumerated and diagnostic features are outlined. In this series basal cell epitheliomas were by far the most frequent malignant lesions encountered, and at least four-fifths of these were seen along the lower eyelid especially about the inner canthus. Early diagnosis and prompt treatment are stressed as particularly essential because, about the eyelids, even the slightest invasion might find some vital tissue involved and thus might greatly complicate therapy.

The method of removing the bulk of the tumor by desiccation and curettement followed immediately by radiation is fully described as the procedure of choice for most cases. Treatment by various types of radiation alone is briefly discussed. Surgery appears to offer least in the treatment of these cases. Complications of therapy and ways to avoid them are discussed.

ADDENDUM

Since this paper was written, one patient who had received three previous treatments had a questionable recurrence at the lower end of the scar farthest from the lid margin. This patient had had an apparent one and one-half year cure up until she was seen this time. This I believe definitely points out that a three year cure rate is imperative in determining cure of cancer about the eyelids.

140 E. 54th St.

14. Driver, J. R., and Cole, H. N.: Epithelioma of Eyelids and Canthi: Report of Series of 324 Cases, Am. J. Roentgenol. **41**: 616-624, 1939.

15. Sharp, G. S.: Treatment of Cancer of Eyelids, J. A. M. A. **111**: 1617-1622 (Oct. 29) 1938.

16. Traub, E. F., and Tolmach, J. A.: Squamous Cell Epitheliomata of Skin of Face: Report of 26 Cases, New York J. Med. **33**: 875-881, 1933.

17. Welton, D. G.; Elliott, J. A., and Kimmelstiel, P.: Epithelioma: Clinical and Histologic Data on 1,925 Lesions, Arch. Dermat. & Syph. **60**: 277-293 (Aug.) 1949.

Gallstones in Old People.—Gallstones are more common in both men and women in their old age than is usually realized. . . . It is hard to believe that any medical management of them is of any value. In the Peter Bent Brigham Hospital series, the hospital mortality of old people with gallstones was 34%, whereas the hospital mortality for all the patients was only 23.6%. There were 455 patients who knew that they had gallstones and were not operated upon; of these, 28 died wholly of causes produced by the stones and 53 others died of other diseases with contributions from the stones. This is a medical mortality rate of 17.8%, which far exceeds what should be expected from surgery. Gallstones seem to enhance cardiac manifestations in old patients who have heart disease, such as angina and auricular fibrillation. Gallstones and their management increase nervous indigestion. Cancer of the biliary system is not found without them. For all these reasons it is good practice to insist on cholecystectomy soon after the presence of gallstones has been established, and not to wait for complications.—R. T. Monroe, M.D., The Effect of Aging of Population on General Health Problems, *The New England Journal of Medicine*, Aug. 20, 1953.

CANCER OF FOREHEAD AND SCALP

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Cancer involves the scalp either as a primary disease, by metastasis, or by extension from an intracranial carcinoma. Primary scalp cancer is a more dangerous disease than is generally accepted, and the incidence of improper management is frequent. Metastasis to the scalp may be secondary to various types of malignant tumors in different portions of the body, especially if the primary tumor is highly malignant. Carcinomas that are known to metastasize to the scalp [1] on occasions are hypernephroma and carcinoma of the stomach, colon, breast, bronchus, thyroid, prostate, and bladder. Montgomery and Kierland [2] emphasized that metastases may be limited to the scalp and that a diagnosis of carcinoma of the internal organs may first be established by recognition of the cutaneous metastasis by means of a cutaneous biopsy.

Primary carcinoma of the forehead and scalp starts as a basal or a squamous cell lesion; it is of unknown etiology. The precancerous dermatoses are encountered much less often in cancer of the forehead and scalp than they are on the exposed surfaces of the body. As a rare happening cancer of the scalp may develop in scar tissue of long standing. The scar may have been caused by trauma, a thermal or chemical burn, lupus vulgaris, localized scleroderma, or tertiary syphilis. Long-standing roentgen dermatitis involving the scalp, forehead, or any region should always be considered precancerous and treated accordingly. Bowen's disease and senile, arsenical, and solar keratoses rarely occur on the scalp. If present, however, they are true precancerous lesions. Epithelial and sebaceous cysts may undergo malignant change. Malignant change may take place in developmental anomalies of the epidermis and/or the adnexal structures of the scalp. Junctional and compound nevi, which may give rise to malignant melanoma, and primary adenocarcinomas of sweat or sebaceous gland origin will not be considered in this paper.

The dermatologist is usually alert in detecting suspicious new growths over the forehead and scalp and loses no time in taking a suitable specimen of tissue for biopsy at the time of the initial examination in order to promptly confirm his clinical diagnosis.

ESTABLISHMENT OF POSITIVE DIAGNOSIS

The diagnosis of cutaneous cancer of the forehead and scalp, as anywhere on the skin's surface, is made on the basis of the results of microscopic examination of a suitable specimen of tissue that is clinically suspected of being malignant. In the large superficial epitheliomas of the scalp, more than one specimen may be required before the diagnosis can be established. The thread-like, slightly elevated, mother-of-pearl-colored border of the lesion is the site most suited for obtaining material for the biopsy. When the possibility of bone invasion by cancer exists, specimens of bone should be taken for study. Roentgen examination of bone is inadequate to differentiate the similar characteristics of osteomyelitis, roentgen necrosis, tumor invading bone, or combinations of these three.

Cancer of the scalp is a more serious disease than is generally considered. Case histories of patients who have cancer of the scalp reveal a tendency for the patient to procrastinate and to delay seeking medical aid longer than he would in a case of similar lesions on the face. Unfortunately, physicians are to blame for allowing many simple, small cancers of the scalp to grow, infiltrate, and become a major treatment problem. Our failure is, first, in having too little suspicion of cancer of the scalp. The physician who makes the initial examination too frequently fails to establish a positive diagnosis by taking a suitable specimen of tissue for biopsy. Second, the incidence of poor management by the physician in scalp carcinoma is greater than that for other regions of the head and neck. Mismanagement of scalp cancer is serious and may add to the patient's disability and the cost of getting well or may indeed lead to his death. We must and can remedy our failure for the delay in establishing a microscopic diagnosis promptly.

CLINICAL FEATURES AND PATHOLOGICAL CHANGES

The clinical features and pathological characteristics of primary carcinoma of the forehead and scalp are essentially the same as those of carcinoma in other portions of the head and neck with few exceptions. Emphasis should be given only to the frequent occurrence on the scalp of basal cell carcinomas of multicentric origin. These lesions grow and involve sizable portions of the scalp's surface. Their most characteristic feature is their thread-like, mother-of-pearl-colored border. The edges of such a lesion may be flat or slightly elevated and rolled. The surface of the lesion may be essentially normal in its appearance or slightly hyperkeratotic and scaly, crusted, moist, erythematous, atrophic, ulcerated; combinations of these features may be present. The hair is usually present in patches and is not destroyed completely by the tumor. Clinically, cancer of the scalp may be mistaken for psoriasis, lupus erythematosus, seborrheic dermatitis, scar, or pyoderma in the moist type of lesion. Small nodular epitheliomas of the scalp may resemble the common mole. Morphea-like epitheliomas have been observed on the forehead and scalp on at least three occasions. Pig-

Drs. W. B. Weary, Charles Martin, R. S. Clayton, and James T. Mills helped in the studies reported and in the preparation of the manuscript.

Read in the Symposium on Cutaneous Malignancy, an Appropriate Segment of Dermatology, before the Section on Dermatology and Syphilology at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

1. Figi, F. A.: Malignant Tumors of Scalp, S. Clin. North America **26**: 859-870, 1946. Symmers, D.: Metastasis of Tumors: Study of 298 Cases of Malignant Growth Exhibited Among 5,155 Autopsies at Bellevue Hospital, Am. J. M. Sc. **154**: 225-240, 1917. Ronchese, F.: Metastasis of the Scalp Simulating Turban Tumors, Arch. Dermat. & Syph. **41**: 639-648 (April) 1940.

2. Montgomery, H., and Kierland, R. R.: Metastasis of Carcinoma to Scalp, Arch. Surg. **40**: 672-684 (April) 1940.

mented basal cell carcinomas of the scalp are rare. Mistaking a malignant melanoma for a carcinoma of the scalp is a serious error that is made too frequently.

ROUTES OF SPREAD [3]

The spread of cancer of the scalp is dependent on many factors, many of which are unknown, variable, and unpredictable. These factors include the type of cells making up the neoplasm, the area in which invasion can occur, the amount of connective tissue response called forth by the invading epithelioma, the direction of the growth, the type of tissue near the new growth, the blood supply or nutritional state of the tissue, the effects of previous therapy, and the patient's age and his general health. Most basal cell cancers grow relatively slowly on the scalp but are invasive and destructive. They reach huge dimensions and may produce a prolonged and serious illness with disfigurement, pain, crippling disability, and even death.

Cancer of the scalp, forehead, and temple has a strong tendency to invade the dermis. This is strikingly exhibited

Fig. 1.—Spread of basal cell cancer through the inner table of the skull includes, *A*, persistent, proliferating cancer involving the soft tissues and bone. Tumor recurred despite x-ray therapy followed by a craniotomy and removal of a 5 by 6 cm. bone flap, and *B*, carcinoma had extended from forehead, invaded the outer table of the frontal bone, and then spread by way of the inner table to the squamous portion of temporal bone. Penetration to the outside involved the region of the ear.

in the older and/or more advanced carcinomas. It occurs, however, in some early lesions. Peripheral and downward infiltration in the dermis is usually not uniform. Invasion may progress several times more rapidly on one side of the lesion than on the other sides. This uneven and ameboid invasion makes it difficult to determine clinically the border between normal and cancer tissue. The larger the lesion, the wider should be the peripheral zone allotted for treatment beyond the visible and palpable extent of the carcinoma.

In cutaneous cancer, there is a strong possibility of peripheral spread in or on the surface of the scalp's fascia. The resistance to spread is apparently less in the fascia than it is in the underlying tissue; thus the lesion is allowed to spread widely and sometimes rather rapidly over the top of the cranium. Primary carcinoma of the temporal region may invade the temporalis fascia and spread peripherally and often downward extending beneath the zygomatic arch to the tendinous insertion on the mandible —all without invasion of the underlying temporalis muscle.

The periosteum offers a temporary restraining effect to bone invasion by carcinoma of the scalp, perhaps because of the greater ease of peripheral travel in this tissue as compared with that in bone. It is difficult and, on occasions, impossible to detect early invasion of carcinoma in the periosteum, except by biopsy.

Some epitheliomas spread along the nerve sheaths of one or more nerves. On rare occasions carcinoma of the scalp spreads by permeation of the small vessels of a lymphatic plexus, or it may follow one or more larger lymphatic vessels or plexuses. Permeation by continuity through lymphatic vessels may be observed in either basal or squamous cell epitheliomas. Squamous cell carcinoma may exhibit peripheral embolic spread. The prognosis of patients with a discontinuous, embolic type of spread of carcinoma is adverse.

Dr. N. A. Thorne presented a case for Dr. W. J. O'Donovan at the Tenth International Congress of Dermatology in London in 1952. The lesion was diagnosed as being carcinoma erysipelatodes secondary to squamous cell carcinoma arising in a wen. The patient in the case presented was a white man 81 years old. In 1932, a swelling developed on the right anterior portion of the scalp, slowly increased in size, discharged on several occasions, and, in 1950, was lanced. In June, 1951, the patient noticed a pink discoloration on his forehead; this spread to his face. Examination revealed ulceration of the wen because of squamous cell carcinoma. The patient's face was covered with telangiectases and a circinate raised erythematous infiltration caused by carcinoma cells in the lymphatics of the dermis. Metastases were present in the cervical lymph nodes. The lymphatic invasion over the forehead and face produced an inflammatory erysipeloid eruption comparable to the inflammatory cutaneous lymphatic metastasis of the chest wall and arm in carcinoma of the breast (carcinoma en cuirasse).

Both basal and squamous cell cancer spread by invasion along the adventitia of arteries and veins and by permeation through the lumens of blood vessels. Adventitial extensions may continue beyond the main mass of the cancer. The tendency for cutaneous cancer to spread in the lumen of the blood vessels is rare. Mohs and Lathrop [4] reported two cases, one of squamous cell cancer with cerebral metastasis and one of the basal cell type in which the veins in the region of the nasolabial fold were permeated and in which, in the deeper portion of the neoplasm, the downward growths were exclusively intravascular. There was no evidence of metastasis after four years.

Permeation of bone by cancer of the scalp is not rare. After invading the periosteum, the progress of the infiltration is in the outer table of the calvarium. The spread may continue both downward and peripherally through the spongy diploë. Such an occurrence should be considered a serious matter. The chances for cure are reduced appreciably when the bone becomes invaded. The neoplasm usually spreads widely over the top of the cranium before

3. Most of the remarks on routes of spread are based on Mohs and Lathrop: Modes of Spread of Cancer of Skin, A. M. A. Arch. Dermat. & Syph. **66**: 427-439 (Oct.) 1952.

4. Mohs and Lathrop.[3]

penetrating the bone. The coronal and other sutures may offer a path of less resistance for intracranial penetration. Expansion through the spongy bone of the inner table may be widespread. The inner table may be a path of least resistance in a few cases of cancer of the scalp involving bone. The following case is an illustration of this mode of spread.

A 44-year-old white woman complained of an ulcer of the forehead. She noticed a small nodule 17 years ago. It grew very slowly and eventually ulcerated; the forehead and eyebrow region on the left were involved. Three years earlier the lesion had been treated with x-ray therapy of unknown quality and quantity. This had given temporary relief, but the lesion had soon recurred. The woman lost 30 lb. (13.6 kg.) in six months, and when first seen she had a contraction of the left upper lid from the lesion above it (fig. 1*A*). Physical examination revealed a flat ulcerated lesion of the left side of the forehead. It was 5 by 6 cm. in diameter, and in the middle there was a deeper ulcer. There was also destruction of the outer table of the skull. Results of serologic tests for syphilis were normal.

From June 26 to July 10, 1947, the patient received x-ray therapy daily except on Sundays. The dose was 300 r in air, with 200 kv. and 0.5 mm. Cu and 1 mm. Al filter to a portal 7 cm. in diameter on the left side of the forehead with a focal distance of 50 cm. (3,600 r total dose). In three months there was no clinical evidence of carcinoma in the ulcer. Because of necrosis of a portion of the denuded bone and accompanying pain, the patient was referred for the removal of the diseased bone. In October, 1947, examination showed a 3 by 8 cm. ovoid lesion on the left frontal area with a zone of hyperemia. Exposed spongy bone was seen at the base of the lesion. Films of the skull showed bony destruction of the left frontal region measuring 3 by 4 cm. This destruction was 3 cm. above the left orbit in about the midportion of the left frontal bone. Several small sequestrums were visualized. The impression gathered clinically and from the films of the bone was that there was osteomyelitis of the left frontal bone involving an area of 3 by 4 cm. A bone biopsy was not done. At operation, bur holes were made in the upper portion of the necrotic bone, and these were enlarged with a heavy rongeur. The sclerotic bone was found to extend 1 cm. beyond the margin of the skin defect. This was all removed leaving a defect 5 by 6 cm. This defect was later closed with a pedicle flap.

For several years there was an apparent cure. Recurrences became evident by February, 1952. On examination a healed skin graft 6 by 8 cm. covering the left side of the forehead was noted. A 2 by 4 cm. ulcer was present in the portion of the graft near the midline and above the left orbit. There was elevation and induration about the ulcer. Coming up from below, without a preceding surface lesion, was a preauricular elevation and induration. Draining, ulcerating areas were noted in the canal and in the preauricular and postauricular folds. The appearance of the left ear was that of a second primary carcinoma of skin of the base of the ear (fig. 1*B*). The skin and subcutaneous tissue between the graft and the preauricular area 5 cm. away were normal clinically. There was a left facial paralysis and horizontal nystagmus.

X-ray examination of the skull showed a craniotomy of the left frontal bone measuring 4 by 7 cm. (fig. 2*A*). The posterior edge of the defect coincided almost exactly with the left coronal suture. The anterior and medial aspects of this defect exhibited a destructive process of the bone that extended practically to the midline and vertically above the rim of the orbit for a distance of 4 cm. There was also evidence of destruction at the superior and along the anterior portions of this craniotomy defect. There was also extensive destruction of the left temporal bone measuring approximately 4 by 5 cm. The bone appeared to be completely destroyed in this area. There were other small destructive lesions in the anterior fossa of the skull on the left side (fig. 2*B*).

From March 1 to March 25, 1952, x-ray therapy was given to a portal 10 cm. in diameter centered over the left ear. A second portal centered over the forehead measured 12 by 10 by 9 by 4 cm. One hundred fifty roentgens in air was given to each portal daily until 3,000 r in air had been given. The factors were 220 kv., with 0.5 mm. Cu and 1 mm. Al filter and 50 cm. skin target distance. Three months later the patient experienced an attack of

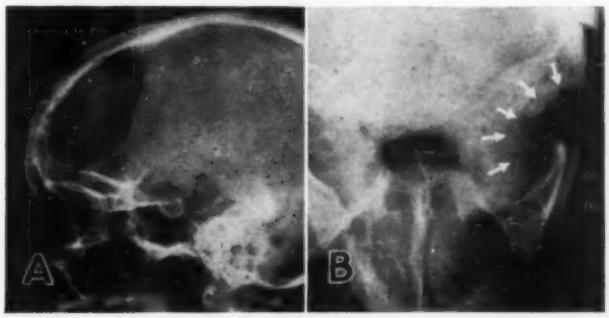

Fig. 2.—*A*, lateral radiograph of skull showing craniotomy defect in the frontal region. A destructive lesion is seen in the anterior inferior margin of this defect involving the full thickness of the skull. Note large area of destruction in squamous portion of temporal bone extending from above and behind external auditory canal forward to a point near the junction of sphenoid wing with lateral margin of the calvarium. *B*, submentovertex projection of the same skull showing an extensive destructive process involving the lateral half of the floor of the middle fossa of the skull (arrows). This defect is continuous with the destructive lesion shown in *A*.

sudden headache, chewing of the tongue, irregular breathing, purple lips, and all the symptoms of an epileptic attack. When the attack ended the patient was in a state of weakness, exhaustion, and disorientation.

Radiographs made in September, 1952, showed the extension of the malignant process into the tables of skull surrounding the defect in the frontoparietal region and posteriorly in the right occipital region. X-ray evidence indicated that a tumor probably surrounded the internal auditory canal and involved the innermost portion of the petrous ridge of the temporal bone. It extended forward to affect the spongy portion of the temporal bone and irregularly to the midline in front to involve the frontal bone. The meninges and brain were invaded as a direct extension and infiltration from cancer of the bones of the skull. The spinal fluid rarely acts as a means of spread for the tumor cells in basal or squamous cell cancer from the scalp. The following case illustrates the continuous invasive and destructive traits of cancer of the scalp.

This 69-year-old white man was seen at the Tumor Clinic, Parkland Hospital of Dallas. When he was 30, a "mole" was noted on the occipital portion of the scalp. The lesion was said to ulcerate and to become infected frequently. There was a gradual enlargement of the lesion over a period of many years. When the man was 66, the lesion was treated by electrocoagulation, and almost complete healing followed. Caustic plasters were applied at intervals for one to two years to the lesion. It had grown at this time to approximately 3 cm. The first hospital admission was in May, 1947, at the Tumor Clinic of Parkland Hospital.

On physical examination the right occipital region of the scalp was found to be the seat of an ulcer that measured 8 by 10 cm. The underlying spongy bone was exposed and appeared darkened and necrotic. The lesion had an elevated, indurated border. The regional cervical lymph nodes were palpable. A roentgenogram was reported to show destruction of the right occipital bone from direct extension of neoplasm. A biopsy report on a portion of the ulcer did not indicate carcinoma. Tissue

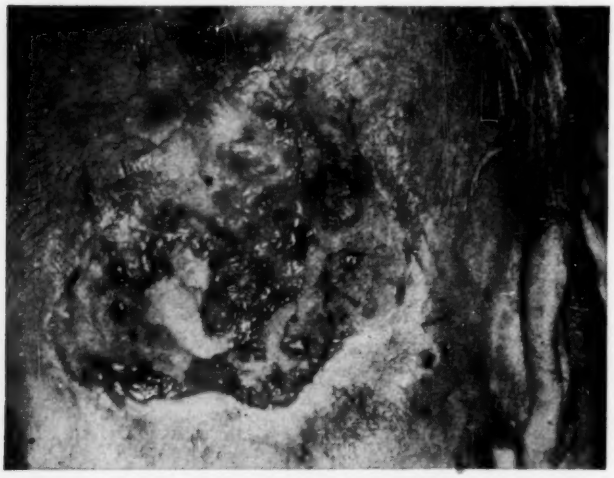

Fig. 3.—Primary basal cell carcinoma with recent transition to high grade squamous cell cancer. Tumor penetrated to the dura in the customary way by infiltration and direct extension of the underlying tissues over a period of years.

removed at subsequent operations was found to contain basal cell carcinoma. The last two specimens examined were reported to be high grade squamous cell carcinoma. The pathologist reported that the cervical lymph nodes did not contain carcinoma. Serologic tests for syphilis were normal.

Two débridement procedures for osteomyelitis of the skull were done in 1947. With the patient under general anesthesia, the outer table of the skull underlying the ulcer was found to be completely necrotic. The defect measured 6 cm. in diameter. There was relatively clean granulation tissue under the necrotic table. The outer table was removed except for a 15 mm. area that was adherent and could not be removed. A split thickness graft from the anterior left thigh was placed over the granulating area. Eight additional operations for removal of necrotic bone and the application of a skin graft were carried out during 1947, 1949, 1950, 1951, and 1952 for what was considered osteomyelitis of the bone. The diseased bone was not examined by the pathologist.

Low intensity radium needles were implanted for seven days along the margins of the ulcer in an effort to destroy recurrent small areas of carcinoma. Three thousand roentgens low voltage unfiltered x-ray therapy was given in 10 days to a 6 by 4 cm. field in 1951 and to a 4 cm. field in 1952; 4,000 r were given to a 3 by 1.8 cm. field and to a 4.3 by 7.5 cm. area. Despite these measures the growth has continued in the bone, has now invaded the dura (proved by biopsy), and has produced a defect illustrated in figure 3.

COMPLICATIONS OF IRRADIATION

Atrophy.—Atrophy of the soft tissues of the scalp may develop, with diminished blood supply to the areas. This may lead to diminished resistance to trauma and/or infection or failure of the area to heal after irradiation.

Bone Infection and Necrosis.—Ewing [5] has pointed out that the blood supply of bone is peculiarly susceptible to strangulation by irradiation. That such changes render membranous bone unusually fertile soil for bacterial invasion and necrosis has been amply demonstrated.[6] Cancercidal doses of radiation may produce enough destruction of the normal immunological barriers to allow the spread of infection from the cranium by retrograde thrombophlebitis.[7]

Susceptibility to Damage.—The tissues of the brain are more susceptible to irradiation damage than has generally been accepted. Convulsions after roentgen therapy occurred in one of our patients. A similar occurrence took place in a patient observed by Driver.[8] The patient received approximately 10,000 r low voltage x-ray therapy to a basal cell cancer measuring 9 by 7.5 cm. on the crown of the scalp. Reflex changes, cerebral hypoplasia, vascular changes, and glial degeneration have been attributed to irradiation.

Commenting on the effects of irradiation on the brain, Dyke [7] described a patient who had received 80 to 90 threshold erythema dose over a period of years. Blindness, convulsive attacks, and also a large ulcer in the scalp and necrosis of the occipital bone subsequently developed. When this patient came to autopsy, approximately four years after the last roentgen treatment was given, the medulla and occipital and parietal lobes of the brain showed hemorrhagic necrosis. Within the areas of necrosis there were decreased reactions of the interstitial tissue, and a deposit of homogenous substances was noted that corresponded to Alzheimer's "colloid degeneration." Dyke stressed that the harmful effects of irradiation on the brain may become manifest 5 to 15 years after treatment and may prove fatal. A number of monkeys that were given irradiation did not show any immediate effect, but later on evidence of degenerative changes in the brain did develop.

Blood Vessel Damage.—Blood vessel damage may lead to necrosis of the tissues supplied by the vessels.

5. Ewing, J.: Radiation Osteitis, Acta radiol. **6**: 399-412, 1926.

6. Desjardins, A. U.: Osteogenic Tumor: Growth Injury of Bone and Muscular Atrophy Following Therapeutic Irradiation, Radiology **14**: 296-308, 1930. Ewing.[5]

7. Dyke, C. G.; in discussion on Pendergrass, E. P.; Hodes, P. J., and Groff, R. A.: Intracranial Complications Following Irradiation for Carcinoma of Scalp, Am. J. Roentgenol. **43**: 214-225, 1940.

8. Driver, J. R.: Personal communication to the authors.

Osteomyelitis.—Osteomyelitis may develop as a result of irradiation of carcinoma of the scalp.

Intracranial Infections.—The following sobering report on intracranial infections is worthy of summary. Pendergrass, Hodes, and Groff [7] reported fatal intracranial complications in three patients who received large doses of radiation for carcinoma of the scalp. The first was a white man, 60 years old, who complained of an ulcer of 11 years' duration. The lesion measured 13 cm. in diameter and was situated over the right frontal bone. The bone in the center of the involved area was denuded. The edges were raised with considerable infiltration evident in the outer canthus and upper lid of the right eye. No metastatic nodes were palpable in the cervical region. The biopsy showed spinocellular carcinoma, grade 2. The serologic examination was normal. On roentgen examination, there was a demineralized area in the frontal bone on the right side caused either by infection or malignant disease, or both. The patient had received an unknown amount of low voltage x-rays for the lesion five years and again two years prior to admission to the hospital. At irregular intervals one year before being seen by Pendergrass, Hodes, and Groff the lesion had been treated with high voltage radiation (200 kv. and 50 cm. skin target distance) receiving a total of 5,000 r filtered through 0.50 to 0.75 mm. of copper.

On admission the treatment was outlined as follows: The entire lesion was divided into six fields, each 7 cm. in diameter. One portal was treated daily, 350 r being delivered at each sitting. The factors were 200 kv. with 15 ma. and a skin target distance of 18 cm. A thoraeus filter equivalent to 5 mm. Cu (1.25 mm. Sn, 0.25 Cu, and 1 mm. Al) was employed. The patient received 2,000 r to each of the six portals in 55 days. Two weeks after the last treatment a biopsy revealed evidence of malignant activity. After consultation with another radiologist, the lesion was given an additional 2,000 r to each of two portals in six days. Evidence of an intracranial lesion developed six weeks after the last treatment. A dural and subdural infection were found and drained. The patient ultimately succumbed to the intracranial infection. A diffuse, purulent meningoencephalitis was found at autopsy. A culture of the material obtained from the cavity in the brain showed both Micrococcus (Staphylococcus) albus and Streptococcus hemolyticus.

Their second patient, a 53-year-old man, was admitted on March 27, 1937, with an ulcer of the scalp of nine months' duration, 10 cm. in diameter, and overlying the left parietal bone. Serologic examination was normal, and roentgen examination of the bones of the vault showed nothing abnormal. The biopsy report on the lesion was squamous cell carcinoma. The lesion was divided into three fields, each 9 cm. in diameter. Four hundred roentgens was delivered through one portal per day until the patient had received 2,100 r in 16 days. The factors were the same as in the first patient. The lesion regressed rapidly. Several metastatic cervical nodes were also given x-ray therapy and subsequently excised; they contained carcinoma cells. Bur holes were drilled in the calvarium to hasten granulation tissue proliferation. Eight weeks after the last treatment, signs of an intracranial infection developed. A subdural abscess from which a culture revealed micrococci was drained, but the patient died. At autopsy a large abscess was found in the brain. Even more unusual was a sizable metastatic nodule in the contralateral temporal lobe. The metastatic focus in the brain merits special comment as similar metastases in patients with carcinoma of the scalp have not been observed. Death in this patient was due to an obliterative endarteritis and brain softening.

The third patient described by Pendergrass, Hodes, and Groff was a 47-year-old man who was admitted on April 12, 1930. Examination revealed an ulcer of the scalp of nine years' duration. The lesion overlying the parieto-occipital region was 4 cm. in diameter. The bone was not exposed, serologic examination was normal, and a biopsy indicated a basal cell carcinoma. The lesion received 2,750 mg. hours of radium in 18 months. Later a recurrence was removed surgically leaving denuded bone. The bone was subsequently spotted with bur holes to promote granulation tissue proliferation. Another recurrence developed; this received 15,800 r of low voltage radiation in five months. The patient received 5,000 r of unfiltered radiation and 2,600 r filtered through 0.25 mm. Cu in four days (physical factors, 135 kv., 5 ma., skin distance 30 cm., field 9 cm., and filtration 0.25 mm. Cu and 1 mm. Al). Six months later another biopsy showed carcinoma, and an additional 7,000 r of unfiltered radiation and 1,200 r with 1 mm. Al were delivered to the lesion in two days. Osteomyelitis of the calvarium developed and progressed until a large portion of dura became exposed. The dura and brain subsequently degenerated. A diffuse, micrococcic meningitis caused death. Autopsy was not performed.

Dr. Cornelius G. Dyke of New York City, in the discussion of the paper by Pendergrass, Hodes, and Groff, pointed out that it was extremely difficult to be certain that the irradiation was instrumental or causative in producing death in these patients by an infectious process. He reported having seen several patients in whom, during the roentgen treatment of a glioma, an epidural abscess developed several weeks or months after the operation. Thirty-one patients were treated in the operating room with 2,000 to 3,000 r 200 kv. (peak) delivered at one sitting by Dr. Dyke. Five of these 31 died of infections. In addition, a number of monkeys were given fairly large doses of roentgen rays, and in 3 out of 10 monkeys infections developed, and the animals died of meningitis or cerebral abscess. His feeling was that radiation in large doses apparently does interfere with the normal protective processes in the body and that some patients so treated are probably a bit more susceptible to infection [9] and more liable to succumb thereto than if not treated in this manner.

TREATMENT

Treatment in General.—The treatment of a patient in whom a diagnosis of cancer of the forehead or scalp has been proved must be individualized. The patient's age, the age of the growth, the rate and the direction of spread

9. Elsberg, C. A.; Davidoff, L. M., and Dyke, C. G.: Roentgen Treatment of Tumors of Brain in Operating Room by Direct Radiation Through Open Wound, Bull. Neurol. Inst., New York 6: 19-32, 1937.

of the growth, and previous treatment must be considered. One must also evaluate the lesion's size, location, and attachments, the extent of invasion, whether bone, dura, or brain substance have been involved, and the possibility that metastasis to the regional lymph nodes has occurred.[10] The smaller the lesion, the better the prognosis and also the better the results of all modes of treatment. This remark certainly holds true for cancer of the scalp and forehead. Lesions that are less than 2 cm. in diameter usually are early lesions, do not invade bone, and are, therefore, curable with low voltage x-ray therapy by the interstitial implantation of low intensity radium needles, by excision and closure of the defect, by electrocoagulation (Sherwell technique), by cutting current excision, or by chemosurgery. The tumor should be completely eradicated by any one of these methods if the physician directing therapy is expert in the application of the method selected.

Wide publicity should be given to the fact that cancer of the scalp should be considered a more dangerous and a more difficult neoplasm to cure than is generally accepted. Wider and deeper coverage of the area calculated to be the extent and depth of the lesion is advocated. The treatment of patients with cancers of the forehead and scalp that exceed 2 cm. in diameter is arbitrarily divided into four groups for the purpose of discussion.

Group 1.—This group includes lesions involving the scalp and subcutaneous tissues but not the periosteum. The larger the lesion, even in carcinoma that has infiltrated only the superficial tissues, the stronger is the indication for a surgical approach.[11] Weary [12] recommends total excision of the large cancerous growths and primary closure of the defect if possible. In discussing his experience with large wounds of the scalp in World War II, he pointed out that many sizable defects of the scalp could be remedied by primary closure. By taking advantage of the scalp's good blood supply and excellent mobility, closure of the defect was possible by employing an elongated S-incision or a sliding H-closure or by using a semicircular sliding graft. Primary closure is usually preferable to skin grafting. The method of repair is dependent on the size and nature of the defect. When grafts are indicated, the order of preference is first for a full thickness, sliding or rotating scalp flap, second for a split thickness skin graft, and third for a full thickness free skin graft.

When an area of scalp exceeding 5 cm. in diameter receives a cancerocidal dose of irradiation, there is an increased susceptibility of the damaged vessels to obliterative changes and occlusion, with the passing of time, resulting in degeneration of the tissues supplied. The possibility of damage to the underlying bone by x-ray and radium therapy for large lesions has already been stressed. X-ray therapy of 140 to 200 kv. quality has been advocated by persons with excellent training in radiation therapy. The question "Does high voltage x-ray therapy have a place in the treatment of cancer of the scalp or is it contraindicated?" needs careful study and appraisal. Low voltage (80 to 100 kv.) x-ray therapy may be used successfully in cancer of the forehead and scalp. A wise therapist will fractionate treatment, will give small doses over a 10 to 21 day period, and will employ x-ray therapy for lesions that do not exceed about 3 or 4 cm. in diameter. Five hundred roentgens given every second day for 9 or 10 treatments (a total of 4,500 to 5,000 r) or 700 r given every second day for 6 or 7 treatments (a total of 4,200 to 4,900 r) is suggested.

When irradiation is contemplated for cancer of the forehead and scalp, the use of low intensity radium needles interstitially has many advantages.[13] A superficial basal cell cancer measuring over 8 cm. in greatest diameter and involving the forehead was treated successfully with low intensity needles and has remained well without sequelae for approximately five years. The patient was treated on an outpatient basis by Dr. J. E. Miller who was then on the Parkland Hospital Tumor Clinic staff. Only one-half of the lesion was treated at a time. After three or four months, the second half was treated; thus a high dose of irradiation in the center of the lesion was avoided. A dose exceeding 12,000 to 14,000 gamma roentgens is thought to be incompatible with viability of the tissues. The use of this method of splitting the area for treatment in large lesions of the scalp may be practical on occasions. The next two case histories also exemplify the usefulness of radium needles.

An 83-year-old white woman sought aid on Oct. 27, 1947, because of a "sore" on the scalp that had been present for five years or more. The lesion had been growing more active during the past 10 months. The patient had taken potassium arsenite (Fowler's) solution for a short period of time many years earlier. No treatment had been given to the lesion. Microscopic study following biopsy showed basal cell cancer. The lesion involved the left parietal area and measured approximately 5 by 5.5 cm. It was irregular in outline. A portion of the lesion was elevated; it resembled granulation tissue. The scalp was freely movable and not adherent or fixed to the bone.

On Oct. 27, 1947, with the patient under procaine anesthesia, low intensity radium needles were implanted in a prearranged pattern to cover the area completely, except for a small superficial projecting portion 1.5 by 1.5 cm. This projection from the main growth was destroyed by electrocoagulation. Eight needles, each containing 2 mg. of radium, and two needles, each containing 1 mg. of radium, were used for the implantation and were left in place for seven days. Healing required two and one-half months. The treated site remained well and asymptomatic for four years until the patient's death from other causes on Aug. 13, 1951, at the age of 87.

A 69-year-old white woman was examined on July 26, 1950, for a "sore" on the frontal portion of the scalp of approximately five years' duration. A specimen for biopsy was taken and the report was basal cell cancer. The lesion measured 2 by 2 cm. and was freely movable. A surface crust covered the shallow rodent ulcer. On Aug. 8, four low intensity radium needles, each containing 2 mg. of radium, were implanted. Three of the needles were im-

10. Michelson, H. E.: Cutaneous Cancer, J. A. M. A. **136**: 683-686 (March 6) 1948.

11. James, A. G.; Anderson, R. G.; Scholl, J. A., and Martin, B. C.: Cancer of the Scalp, Am. J. Surg. **80**: 441-445 (Oct.) 1950. New, G. B.; Figi, F. A., and Havens, F. Z.: Replacement of Tissues of Forehead and Scalp, S. Clin. North America **14**: 607-613, 1934.

12. Weary, W. B.: Personal communication to the authors.

13. Martin, C. L.: The Layer Technic in Radium Needle Therapy, Am. J. Roentgenol. **48**: 377-383, 1942; Low Intensity Radium Element Needles: Janeway Lecture, 1949, ibid. **62**: 467-492, 1949. Howell, J. B.: Cancer of the Center Face, South. M. J. **43**: 283-291, 1950.

planted 1 cm. apart to cover the base of the lesion, and the fourth needle was placed perpendicularly to the ends of these three needles. The needles were sutured in place and allowed to remain for seven days. Healing required two months. The cancer was destroyed by this treatment, and the treated area has remained well for approximately three years.

In our experience the most satisfactory results in the management of large lesions in group 1 have been by surgery. The following brief case history illustrates the good results from this method. A 54-year-old woman was seen first in 1938 at the Tumor Clinic of Baylor Hospital. At that time she complained of a sore on her forehead of some 20 years' duration. On examination of the forehead, there was noted a circular lesion 4 cm. in diameter to the right of the midline of the forehead. The upper portion was covered with a crust and extended into the hair. The lower portion was red, and the covering epithelium was atrophic. X-ray examination of the skull on Oct. 6, 1938, revealed no evidence of involvement of the bone by carcinoma. Approximately 15 years earlier x-ray therapy had been given to the lesion on the right side of the forehead for cancer. After the x-ray therapy, there was improvement or complete regression of the central part of the growth. Some seven to eight years later the lower edge of the originally treated tumor had expanded and affected the forehead above the right eyebrow. X-ray therapy of unknown amount and quality was used to treat this lesion, and the patient did not return to the Tumor Clinic until 1946. At this visit a large crusted and scaly area involving the right scalp was seen. Several specimens of tissue for biopsy were taken before the diagnosis of basal cell carcinoma of multicentric origin was made. The Tumor Clinic panel, in evaluating treatment for this case, advised excision of the defect with closure by a skin graft. It was felt that the periosteum and bone had not been invaded. On July 21, 1947, with the patient under general anesthesia, the lesion was surgically excised. It measured approximately 10 by 14 cm. The excision was carried down to the galea. A split thickness graft approximately 1/15,000 of an inch thick was used to cover the defect. Healing was very satisfactory, and the graft took almost completely. There hs been no indication of a recurrence or persistence of the carcinoma during the past six years.

Dr. Clark Finnerud [14] has described a case very similar to the one just mentioned. The lesion, which measured 8 cm., was an extensive basal cell carcinoma of the superficial type involving the forehead and scalp but not invading the bone. The patient was referred for excision and the defect covered with an appropriate graft. The patient has remained well to date.

Group 2.—This group includes lesions involving scalp, subcutaneous tissue, and periosteum but not involving bone. The treatment is primarily surgical. Irradiation is not advocated. Mohs has demonstrated the usefulness of chemosurgery for lesions in this group.

Weary [12] stresses the importance and advantages of complete excision of the neoplasm followed by primary closure of the scalp defect. He emphasizes that undermining the normal scalp allows the wound to be closed, even when the defect at first may appear too large for primary closure. The elongated S-incision, the sliding H-closure, or the semicircular sliding graft has been found to be of special service. Whenever grafts are required, a full thickness or pedicled graft is preferable for the forehead and nuchal area, and for the scalp a full thickness pedicled scalp flap is best.

Attention is directed to the importance of microscopic examination of bone by a competent, understanding pathologist in cases in which bone invasion by the cancer needs to be confirmed or denied. Multiple specimens of bone are required on occasions. Where there is doubt that the process is osteomyelitis, more than a single examination may be needed before planning a radical operation for removal of an area of devitalized bone or an area of osteomyelitis. It is of the utmost importance to stress again the inadequacy of x-ray examination of the skull in differentiating radiation necrosis, osteomyelitis, and invasion of bone by cancer.

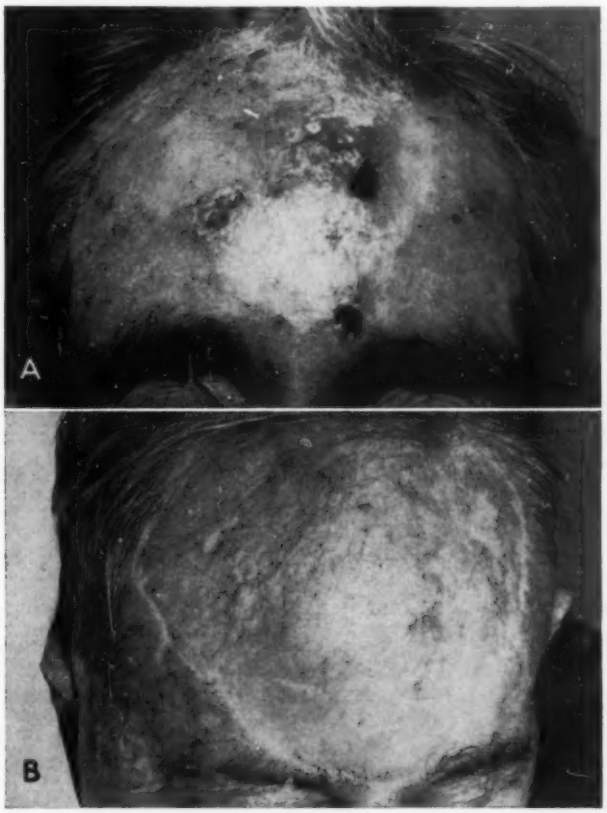

Fig. 4.—Superficial Epitheliomatosis: In basal cell epithelioma of multicentric origin, *A*, lesion has been present 16 years, measures 10 by 14 cm., and in one small area near the midline has invaded periosteum, and, *B*, three years after excision of the tumor and repair of the defect with a split thickness skin graft.

The following case histories are illustrative. A 69-year-old man was seen at Parkland Hospital Tumor Clinic on April 15, 1945, because of a crusted, ulcerating growth on the forehead and scalp (fig. 4). The lesion measured approximately 10 by 14 cm. and had been present since 1934. It was first noted when the patient accidentally skinned his forehead while plowing. A serologic test for syphilis was normal, and microscopic study after biopsy showed basal cell carcinoma. The scalp was freely movable everywhere.

On an experimental basis, the upper half of the lesion was treated by daily application of a 20% concentration

14. Finnerud, Clark W.: Personal communication to the authors.

of podophyllum resin (podophyllin) in alcohol for two weeks. Pain resulted from the paintings. After a rest period of two or three weeks, the lower portion of the growth was treated by the daily application of 20% podophyllum resin in alcohol. After only four or five daily applications, conjunctivitis with a corneal ulcer involving the left eye occurred. After the development of the corneal ulcer, this method of treatment was abandoned. The conjunctivitis and corneal ulcer healed without sequelae, but the carcinoma was not favorably influenced.

On Feb. 17, 1950, with the patient under general anesthesia, the large lesion was excised down to the periosteum. A split thickness graft was used to cover the defect. The skin graft was 1/15,000 of an inch thick and was taken from the right thigh. The grafting was successful. On Aug. 13, 1950, a 1 by 1.5 cm. hard nodule was detected on the left side of the forehead. This was suspected of being a persistent tumor. On Sept. 18 with the patient under local anesthesia, this lesion was excised widely and down through the periosteum. A small portion of the outer table of the frontal bone was chiseled away. The defect was closed by a split thickness graft. The tissue report was basal cell carcinoma in the scalp. The bone was not examined. The forehead has been inspected regularly and has remained well for three years.

A 55-year-old white man was examined on April 4, 1950, because of an ulcer of the left side of the forehead. The lesion had been present eight or more years. It had been treated with x-ray therapy of unknown amount and quality by a general practitioner four years earlier. Three years ago the lesion had been treated by electrocoagulation, but it had persisted. On examination, the right side of the forehead was noted to be involved by a morphea-type basal cell carcinoma measuring approximately 6 by 5.5 cm. A portion of this plaque-like lesion was ulcerated. The lesion was fixed to the underlying bone and was not movable in the areas overlying the ulcers. Consultation with a plastic surgeon was arranged. He advised a wide excision of the cancer, namely the right half of the forehead, with the excision being carried down to the outer table and the soft tissues being removed subperiosteally. The defect was to be covered later by a skin graft.

This lesion, including a generous margin of tissue on all sides, was excised on April 7, 1950. Five sections of the outer table of the skull were taken for microscopic examination to determine whether invasion of bone had occurred. Cancer could not be found in the bone specimens. Granulation tissue sufficient to support a split thickness graft failed to fill the wound during the five months after excision of the cancer. On Sept. 22, 1950, with the patient under general anesthesia, the outer table of the exposed bone was chipped away exposing the medullary cancellous bone. Granulation tissue appeared in four to six days. On Sept. 28, 1950, with the patient under general anesthesia, the surgeon cut a half drum of skin from the right flank with a Padgett dermatome. The forehead wound was then débrided, and more of the outer table of bone removed in several areas; the graft was cut to pattern and sewed into the defect. The graft took well and healing progressed slowly but completely. The treated site has remained well for approximately three years. At a recent inspection of the treated area, there was no indication of a persistence of the carcinoma.

The morphea-like epithelioma presents special treatment problems. This lesion should be treated only by excision or by the implantation of low intensity radium needles. Wide publicity should be given to the fact that this relatively rare type of [illegible]rhous cancer of the skin is curable with low intensity [illegible]ium needles used interstitially. Three such lesions on [illegible]e forehead have been treated successfully by using low intensity radium needles. During a follow-up period of approximately three years, no recurrences have been observed on these patients. Four other persons with morphea-like carcinomas over the head and neck regions have been treated successfully with low intensity radium needles. If this technique is not available or applicable, surgical excision is advisable.

Group 3.—This group includes lesions of the scalp that involve bone but not the meninges. When bone is invaded by cancer from the scalp, the management should be surgical, and the patient should be attended by a neurosurgeon.[12] Radiation has been demonstrated to be ineffective; it has no selective destructive effect on the cancer that has invaded bone. The use of radiation in cauterizing quantities to destroy the invading cancer and bone is dangerous and inferior to present-day neurosurgical management.

The surgical principles in treatment are (*a*) complete removal of the diseased bone (débridement is essential), (*b*) microscopic control, and (*c*) primary closure of the defect if possible or the use of a rotating scalp flap if the defect is too large. Rather than delaying plastic repair 6 to 12 months to rule out persistent carcinoma, as some suggest, Weary advocates primary closure of the defect, if possible, or the use of the proper type of graft promptly. Frequent x-ray studies of the margins of the bone defect combined with clinical examination of the soft tissues will suggest or rule out persistent carcinoma. After 12 to 18 months, if there is no evidence of persistent carcinoma, cranioplasty with a tantalum plate to repair the bone defect may be carried out if desired.

Group 4.—This group includes lesions of the scalp that have penetrated to the meninges and/or brain. The treatment is surgical. A craniotomy should be done, and a bone flap extending well beyond the area of involvement should be removed. The involved bone and dura are removed as a block resection including generous margins of normal surrounding tissue. If the cortex is involved, the diseased area and an adequate margin may be removed by sharp dissection depending on the region of cortex involved. The dura should be replaced by a fascial graft followed by primary closure of the defect. For plastic repair, a full thickness pedicled scalp flap should be used.

SUMMARY

The relatively common primary sources of metastatic carcinoma of the scalp are listed. A brief résumé of the clinical variants of primary carcinoma of the scalp is given, and the importance of basal cell epithelioma of multicentric origin is emphasized. The natural course of the disease is discussed, and the routes of spread are pointed out. The dangers and complications of irradiation in the treatment of large cancers of the scalp are reviewed. The controversial subject of present-day treatment of large cancerous lesions involving the scalp is discussed.

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ROENTGEN IRRADIATION IN THE TREATMENT OF EPITHELIOMA

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and
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For 25 years we have been using both radiotherapy and surgery for the treatment of skin cancer. After treating thousands of patients during this long period, we still use both. Both methods are good, both are reliable in experienced hands, and both regularly produce a perfect cure on scheduled time. Sometimes one method is more suitable than the other; sometimes a combination may be used, or one can use electrosurgical methods. The modern dermatologist is experienced in all of these modalities. There are many reasons why x-ray therapy is used so widely for skin cancer. In the first place, it is successful. It is also painless and bloodless. These facts appeal to patients, especially those who are old or in poor health. From a scientific viewpoint radiation treatment also has advantages. It is possible to cover a wider field about the edges of the cancer than that usually accomplished with surgery. The less the surgeon cuts beyond the visible border of the growth the better his cosmetic result will be. The more he cuts the more difficult the operation becomes. Thus, x-ray, and especially radium therapy cover a wider area and for this reason are more likely to destroy outlying cancer cells and to have a completely lethal action on the tumor.

Morphological reconstructions of skin cancers show that they extend from the primary site (or sites) in the skin in no uniform pattern. Some are shaped like icebergs, just a little showing at the surface and spreading out widely below the surface. A wedge-shaped surgical excision is just the wrong method to use for the iceberg type. Some are shaped like tinker toys, with strands of tumor cells running off from the visible skin lesion and with deeper nodules at the ends of these strands or connected by these strands. The shapes are of an infinite variety, and frequently the changes that indicate extension into the nearby skin are scarcely perceptible and only recognizable by a dermatologist specially trained and experienced in this field. In another type, the superficial epithelioma may extend within the epidermis or in a multicentric manner for several centimeters outside the discernible skin tumor into apparently normal skin. For these reasons the customary excision may be inadequate and the wider field covered by x-ray therapy is advantageous.

DIVIDED DOSE TECHNIQUE

Like all branches of science, radiotherapy has improved greatly in the last 30 years. As far back as 1923 it was known that 10 erythema doses of x-rays were required to kill cancer cells, but then we did not know how to give such a dose without injuring normal tissues and causing skin necrosis. It is only in the last 15 years that the divided dose method of x-ray therapy has been developed so that such a large dose can be given without simultaneous destruction of normal tissue. In 1925 we used a single so-called massive dose of 2½ erythema doses, roughly the equivalent of 1,000 r. This illustrates the tendency in those days to use doses that were too small and to produce an unsightly atrophic scar by giving a single dose instead of divided doses. With the modern technique that we have used for the past 15 years, the total dose averages 5,000 r or more. It is divided into 8 to 10 treatments, so that the cosmetic result is perfect. The fractionization of radium and x-ray dosage makes it theoretically possible to maintain for one to several weeks a saturation dose lethal to cancer cells in the tissues. Since cells are especially susceptible to x-rays during mitosis, this method of irradiation is highly destructive to cancer. Pathological cells are in general more radiosensitive than normal cells, and cells of the embryonal type, or young, actively growing neoplastic cells, are more sensitive than well-differentiated or normal cells.

The total number of roentgens is influenced by the size of the field. The larger the field the more secondary radiation occurs from the iron in the blood and from other tissue elements. Therefore, the lethal dose that is required to kill the cancer cells is less measured in air when the field is large. Experience has shown that for epitheliomas 1.5 cm. or less in diameter the total dose should be 6,000 r at 100 kv. (half value layer 1 mm. Al). Some very superficial basal cell epitheliomas of this size may be treated by 8,000 r at 60 kv. (H. V. L. 0.7 mm. Al) or by Philips contact x-ray at 45 kv., using 10,000 r (H. V. L. 0.55 mm. Al). Failures are always due to improper technique and usually fall into two categories, that is, insufficient field about the visible part of the tumor and incorrect appraisal of the depth to which the lesion extends. For the latter reason we generally prefer to use at least a quality of H. V. L. 1 mm. Al and sometimes H. V. L. 4.4 mm. Cu (140 kv. 0.25 mm. Cu + 1 mm. Al filter). For larger lesions the total dose is lessened. Lesions from 1.5 to 3 cm. in diameter usually receive a total of 5,000 r at 100 kv. (H. V. L. 1 mm. Al). Softer qualities of radiation generally should not be used for such large lesions unless they are definitely of the superficial type. For tumors over 3 cm. in diameter the total dose may be lowered to 3,000 or 3,500 r, depending not only on the size but also on the location and bulk.

A common place for skin cancer to develop is at the inner canthus of the eye. This location presents the danger of spread into the orbit and ultimate destruction of the orbital contents. Surgical removal may necessitate repair of the lower lid and may injure the lacrimal duct. X-ray treatment usually prevents these two hazards, and for old persons it is simpler and easier. The eyeball is amply protected by a metal shield placed beneath the

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lids, and the dosage is fractionated. One usually uses a long anode-skin distance to minimize the irregularity in contour. Sometimes such lesions extend over the root of the nose to the opposite side. These lesions are treated by alternating exposures, first to one side and then to the other. For small epitheliomas on the edges of the lids Philips contact therapy is ideal.

Approximately one-quarter of all skin cancers occur on the nose. There are so many differences as to size, depth, location, involvement of cartilage, ulceration, kind of previous treatment, age of patient, and other more or less important factors, that too much generalization might lead to misconceptions. Small epitheliomas in healthy persons may be readily excised. I treat other epitheliomas—that is to say, the larger, deeper ones, especially in the aged—by x-rays. Roentgen therapy, generally speaking, is the best method of treatment for epitheliomas on the nose and gives excellent results on large epitheliomas, usually far superior to the results of surgery.

RESULTS IN ONE THOUSAND CASES

Unfortunately through the years, owing to lack of space, we have thrown away charts of patients who died or were free from recurrence for over five years in order to clean out our files of inactive charts. This was a serious mistake, but it is still impossible to obtain storage space in the cellar of our building. What actually happened was that the charts of the patients we cured were in time thrown out, whereas those of patients we did not cure were kept in our files. We are, therefore, in a weak position regarding statistics. We have, however, taken at random 1,000 reports of cases of epithelioma from our files. Of these, 410 cases were proved by biopsy. Two hundred twenty were followed for five years or more. In the 1,000 patients there were recurrences after treatment in 3.5%. These were later cured by other means. Various forms of treatment were used. Three hundred sixteen patients were treated by surgical excision, 103 by electrosurgery supplemented by irradiation, and 581 by irradiation alone. Of those followed five years or more, several were treated by radium or x-ray techniques that were entirely inadequate according to modern standards and are now obsolete. The five year cure rate in the 220 patients was, therefore, only 93%, in contrast to 96% for those patients of this group treated by surgical excision and to 97.5% for the 316 patients treated by surgical excision out of the 1,000 cases selected for analysis. We had a little over 98% of cures in 438 patients after treatment by divided doses of roentgen rays with the modern technique of 8 to 10 treatments totaling 3,000 to 6,000 r (or more with the Philips contact x-ray machine or other soft qualities of radiation, produced at 45 to 60 kv. and having a half value layer of 0.3 mm. to 0.55 mm. Al). Two hundred seventy-eight of these patients were treated five or more years ago. It is, however, impossible for us to claim these figures, since we have not been able to contact many of the patients recently.

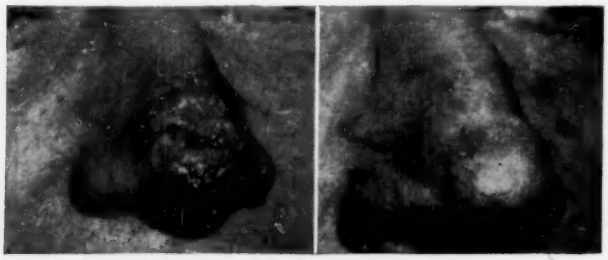

Fig. 1.—Basal cell epithelioma, treated with 8 × 650 r, H. V. L. 1.0 mm. Al, before and seven months after treatment.

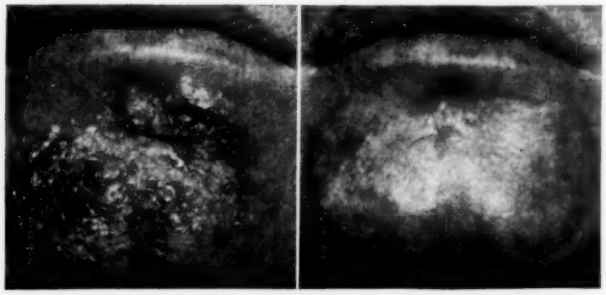

Fig. 2.—Squamous cell epithelioma, treated with 10 × 500 r, H. V. L. 1.0 mm. Al, before and two months after treatment.

The records of many have been lost, and many have changed addresses or have died of old age or other causes. We can claim verified complete cures of over five years in only 98.9% of 94 patients treated by the modern x-ray divided dose technique.

Of the 410 patients who had biopsies, 333 (81%) had basal cell epitheliomas, 57 (14%) had squamous cell epitheliomas, 20 (5%) had basosquamous mixed or transitional or Bowenoid. Of the 590 patients who did not have biopsies, the clinical diagnosis was basal cell epithelioma in 514 patients (86%), squamous cell epithelioma in 68 patients (12%), and 1.5% in the group with mixed cell epithelioma. These figures substantiate the accuracy of clinical diagnosis, the largest error being in mixed cell cases.

Of the 1,000 patients whose cases were analyzed it is interesting to note that over 50% were 60 years of age or older. Two hundred fifteen (21%) were over 70 years of age. The sex ratio of the 1,000 patients was 5 males to 4 females. Forty-six epitheliomas (4.6%) were located at the inner canthus and 229 (23%) were situated on the nose. Only one of the 1,000 patients had radionecrosis or undesirable injuries from the treatment. He was treated by radium in 1939 by a now obsolete technique for an epithelioma of the ear. The injured portion of the helix was later excised.

115 E. 61st St. (21) (Dr. Andrews).

Vaccination During Pregnancy.—Vaccination of a pregnant woman may, though very rarely and perhaps only in special circumstances, lead to fatal generalised vaccinia of the foetus. Vaccination of a pregnant woman during the first trimester of pregnancy, and especially during the second and third months of pregnancy, significantly increases foetal mortality.

If these findings are confirmed by others, it will be clear that vaccination should never be done during the first trimester of pregnancy as part of routine public protection, and that it should be done at this stage of pregnancy only in women who have been in contact with smallpox. Damage to the foetus is done, however, only during the first trimester of pregnancy, and there is virtually no risk from vaccination during the later months.—Patrick MacArthur, M.D., Congenital Vaccinia and Vaccinia Gravidarum, *The Lancet*, Dec. 6, 1952.

RHEUMATIC AND FEBRILE SYNDROME DURING PROLONGED HYDRALAZINE TREATMENT

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Recent experience has extended and confirmed our impressions of the effects of treatment of hypertension with hydralazine hydrochloride (1-hydrazinophthalazine, Apresoline [1]) as the sole antipressor agent.[2] A favorable result is commonly observed; the untoward toxic side-effects, formerly described, appear and usually disappear as the drug is used. In the doses used, tolerance, which others [3] using smaller doses have observed, is rare. Some patients have become slightly anemic, partly, it would seem, as a result of anorexia, but severe anemia [4] is exceptional.

Another striking complication of treatment has appeared in some of our patients; this seems to be related to the use of large doses of hydralazine over long periods of time. The syndrome in its less severe form resembles rheumatoid arthritis; in its severer febrile aspect, it simulates acute systemic lupus erythematosus. It is described in this report because of the natural interest attached to a complication of treatment with a drug in common use and because of its possible bearing on the pathogenesis of systemic lupus erythematosus.

METHOD OF STUDY

The report is based on observations in 13 of 139 patients being treated with hydralazine as the sole antipressor agent. The severity of hypertensive disease was estimated, and the disease type was classified, as previously described.[2] The severity index [5] is adjusted so that the patients with the severest disease score a maximum index of 16 and those with the least disease score an index of 1. The classification and severity index were established during a control period of outpatient or hospital observation; the therapeutic response was evaluated by regular observations of various aspects of cerebral, cardiac, and renal vascular function.[2] Treatment of these 139 patients with large doses of hydralazine (400-800 mg. daily) over long periods of time was considered desirable because favorable control of arterial pressure and vascular disease was obtained in most of them.

Of the 13 patients in whom the syndrome developed, 11 showed excellent control of arterial pressure; diastolic pressure was persistently below 100 mm. Hg in 8, and it averaged 100 mm. Hg in 2 and 105 mm. Hg in 1. Of the two patients with unsatisfactory responses, one showed a drop in diastolic pressure from 125 to 115 mm. Hg; the other patient had a drop in diastolic pressure from 130 to 100 mm. Hg, but, after three months, the pressure slowly rose to pretreatment levels.

The onset of the syndrome, in either its rheumatoid or its febrile form, prompted a variety of special studies. Roentgenograms were made of involved joints and systems, biopsies were taken of inflamed tissues and, in some cases, of muscle; other studies included white and red blood cell counts, measurements of hemoglobin level, sedimentation rate, serum polysaccharide, serum protein (by electrophoresis), and searches for L. E. factor [6] by the dog-marrow, patient-plasma method and by examination of the bone marrow for L. E. cells.[7] In patients with the febrile illness, additional studies included cultures of urine, blood, and pleural and pericardial fluids, examination of sputum, and, in one case, examination of gastric washings, as well as a battery of agglutination tests and skin tests for tuberculosis and histoplasmosis.

THE SYNDROME

The illness that developed in the 13 patients appeared in a mild rheumatoid and a severer febrile form; reasons for supposing that these two were expressions of a single disease are noted below. That this illness was a result of maintenance with large doses of hydralazine over long periods of time seems very likely; it was not observed in patients followed over a shorter mean period. The mean time of onset in the group was 12 months after starting hydralazine treatment; the longest interval in the group was 22 months, although in this patient the 22 months were not continuous, since treatment had been interrupted between the 15th and 18th months. The average maintenance dose was 640 mg. daily; dosage was constant except in one patient who varied his dose irregularly from 200 to 800 mg. and in one whose treatment was suspended for three months.

The types of the hypertensive disease varied widely and included the diencephalic syndrome, renal hypertension, mild and severe essential hypertension, and hypertension in its malignant phase. The severity index ranged from 2.2 to 9.6; neither type nor severity influenced the onset of the syndrome. Responsiveness to the antipressor effect of the drug did not seem to be a factor; only exceptionally did a patient (in this group) who did not respond favorably continue to receive the drug

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From the Research Division of the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute.

Dr. E. L. Posey of Jackson, Miss., supplied the clinical and laboratory data on the acute phase of the illness of the patient in case 2.

1. This product was supplied by Ciba Pharmaceutical Products, Inc.
2. Taylor, R. D.; Dustan, H. P.; Corcoran, A. C., and Page, I. H.: Evaluation of 1-Hydrazinophthalazine ("Apresoline") in Treatment of Hypertensive Disease, A. M. A. Arch. Int. Med. **90**: 734 (Dec.) 1952.
3. (*a*) Grimson, K. S.; Chittum, J. R., and Metcalf, B. H.: Actions of 1-Hydrazinophthalazine (C-5968) on Vasomotor Reflexes and Hypertension in Dogs and Man, Fed. Proc. **9**: 279, 1950. (*b*) Johnson, R. L.; Freis, E. D., and Schnaper, H. W.: Clinical Evaluation of 1-Hydrazinophthalazine (C-5968) in Hypertension: With Special Reference to Alternating Treatment with Hexamethonium, Circulation **5**: 833, 1952.
4. Kaufman, M.: Pancytopenia Following Use of Hydrallazine ("Apresoline"): Report of Case, J. A. M. A. **151**:1488 (April 25) 1953.
5. Severity index is calculated from a summation of all clinical and laboratory findings of four panels: blood pressure, degree of cardiac, renal, and cerebrovascular disease. Each panel contributes a maximum score of four.
6. Haserick, J. R., and Bortz, D. W.: Normal Bone Marrow Inclusion Phenomena Induced by Lupus Erythematosus Plasma, J. Invest. Dermat. **13**: 47, 1949.
7. Hargraves, M. M.; Richmond, H., and Morton, R.: Presentation of Two Bone Marrow Elements: "Tart" Cell and "L.E." Cell, Proc. Staff Meet., Mayo Clin. **23**: 25, 1948.

for long periods. The syndrome arose independently of the presence, nature, or severity of initial toxic symptoms. Allergic diatheses did not seem to cause predisposition to the syndrome; only 6 of the 13 patients gave any indications of allergic disorders in themselves or their relatives; 1 had had contact dermatitis, 1 had had urticaria, and 2 had relatives with asthma. Less convincingly one had had rheumatic fever as a child, and one gave a history of migraine.

The Rheumatic Phase.—The rheumatic phase appeared in all 13 patients (table 1) as a complaint of migratory arthralgia, which was most frequent and most persistent in the interphalangeal joints of the hands and less commonly in the wrists, elbows, shoulders, and knees. Only rheumatic manifestations developed in eight patients (table 1, *A* [rheumatic phase]). The involved joints were stiff and tender; those more severely affected (interphalangeal joints and wrists) became red and swollen and warm; the fusiform swelling of interphalangeal joints resembled that of rheumatoid arthritis (table 1, *A*). Roentgenograms of involved joints showed only soft tissue swelling.

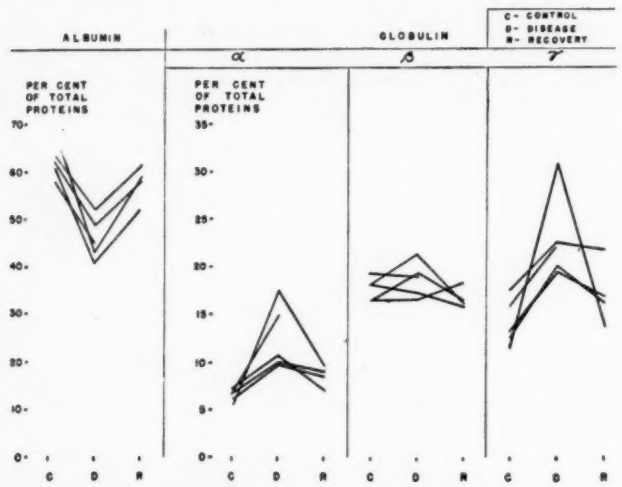

Fig. 1.—Percentile concentrations of albumin and globulin fractions of serum proteins before (C), during the height of (D), and after recovery (R) from the febrile phase of the hydralazine-induced syndrome. Similar changes were found in three patients with the rheumatic phase of the disease.

Sedimentation rates were elevated in four patients, and serum polysaccharide concentration increased in three. The blood hemoglobin level fell from 13.4 to 11.5 gm. per 100 ml. in one patient, and the white blood cell count fell from 8,350 to 4,500 per cubic millimeter in another (table 2, *A*). Proteinuria, hematuria, and cylindruria did not increase during the illness; these sometimes tended to improve; thus two patients showed significant reduction of proteinuria and five a decrease in hematuria.

The most impressive laboratory evidences of this illness were found in the changes in serum protein distribution, as measured by the Tiselius method, in three patients. These were similar to those found in patients in whom the severe febrile phase of the illness developed. They consisted of a decrease in serum albumin and increases in alpha and gamma globulins; thus, the third patient showed a decrease in albumin from 62 to 49% of total protein, an increase in alpha globulin from 6.7 to 10%, an insignificant change in beta globulin (increase from 18 to 21%), and an increase in gamma globulin from 12.8 to 19.6% of total protein. Similar changes occurred in the fifth and eighth patients, and changes of this sort occur in acute systemic lupus erythematosus.[8] What seemed to be a transition into the febrile form of the disease was seen in one patient, whose joint symptoms were accompanied by chills and temperature to 102 F. The temperature fell when hydralazine therapy was discontinued, and fever recurred when the drug was given again.

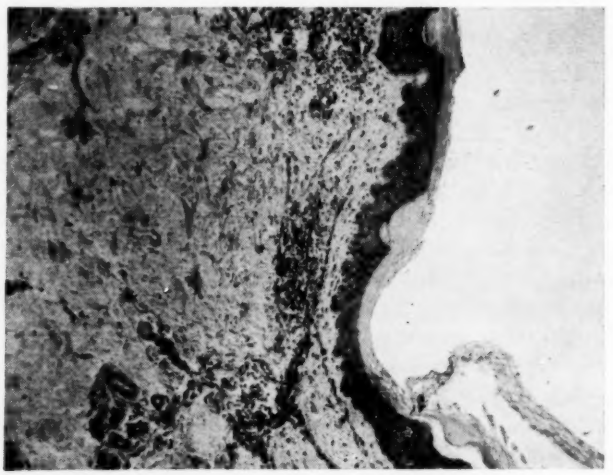

Fig. 2.—Irregular collections of inflammatory cells in the upper cutis; included are polymorphonuclear leukocytes, lymphocytes, eosinophils, and stroma cells. There is slight edema of collagenous areas. The diagnosis was nonspecific dermatitis of the erythema group.

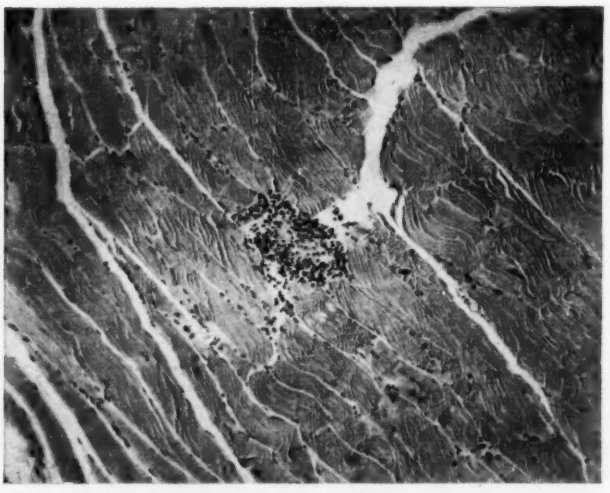

Fig. 3.—Lymphorrhagia throughout the muscle and particularly around blood vessels. The collagen is normal. This nonspecific reaction is seen in rheumatoid arthritis, rheumatic fever, dermatomyositis, and systemic lupus erythematosus.

The course of the illness in the eight patients whose manifestations were primarily rheumatic, including the one who had fever, was characterized by joint pains that were, on the whole, severer than in those who went on into the febrile phase. Four of the eight patients were disabled by arthritis.

8. Lewis, L. A., and Haserick, J. R.: Unpublished data.

TABLE 1.—*Symptoms and Signs in Thirteen Patients Receiving Hydralazine*

Patient	Sex	Age	Pretreatment Severity Index, 0-16	Average Diastolic B. P., Mm. Hg		Early Toxic Symptoms	Daily Dose Hydralazine, Mg./Day	Asymptomatic Treatment Period, Months	Symptoms and Signs	Duration of Symptoms After Hydralazine Therapy, Days	Exacerbating Dose of Hydralazine, Mg./Day
				Control	Drug						
						A. Rheumatic Phase					
1	F	48	8.8	130	100	Headache, palpitation	500	6	Painful, red swollen joints, hands, wrists; stiffness of elbows and shoulders	1	200
2	M	45	7.4	125	115	None	700	6	Pain and stiffness of all joints	28	200
3	M	57	8.4	117	95	Burning of face	400	9	Stiff, painful, swollen joints, hands, and wrists; chill; temperature to 102 F	28	100
4	F	44	5.8	130	105	Chills, fever, headache	600	9	Stiff joints, especially hands and wrists	14	200
5	F	41	8.8	130	95	Headache	800	7	Stiff, painful joints; fusiform swelling of hand and wrists	8	200
6	F	58	2.2	110	90	Dizziness	700	11	Stiff, painful joints; fusiform swelling of hand and wrist joints	1	200
7	M	40	7.8	118	100	Headache, vomiting, purpura, fever, thrombophlebitis	800	12	Stiff, painful, red swollen fingers; stiffness of knees	2	200
8	M	47	8.2	120	90	Headache	800	13	Stiff, painful, swollen joints, wrists, and fingers	Not discontinued	...
						B. Febrile Phase					
9	M	46	9.6	122	90	Nausea	800	18	Discomfort of joints of hands; erythema of hands and forearms; fever; prostration	7	No recurrence 200
10	M	60	7.6	122	85	None	800	18	Stiff, swollen finger joints; dyspnea; weakness; abdominal pain; fever; pleural and pericardial effusion	21 terminated with corticotropin	No recurrence 200
11	M	38	8.8	126	80	Burning of face, palpitation	800 (6 mo.) 600 (5 mo.)	11	Painful, red swollen finger joints; chest and abdominal pain; fever; prostration; pleural and pericardial effusion	14	600
12	M	52	9.4	150	100-130	Anorexia, conjunctivitis	800 (14 mo.) 0 (4 mo.) 500 (4 mo.)	22	Painful, red swollen finger joints; fever; muscle and substernal pain; pleural and pericardial effusions	Persisted until treated with corticotropin	...
13	F	36	9.6	135	80	Headache, palpitation, nausea, and vomiting	600	17	Painful, red swollen finger joints; fever prostration; cough; pneumonitis	7	...

TABLE 2.—*Laboratory Observations on Thirteen Patients Receiving Hydralazine*

Patients	L. E. Test		Serum Polysaccharides, Mg./100 Cc.		Erythrocyte Sedimentation Rate, Mm./Min.		Blood Hemoglobin Level, Gm./100 Cc.			White Blood Cell Count, No./Mm.³			Urinary Proteins, Gm./24 Hr.			Urinary Tubular Casts, Millions/12 Hr.			Urinary Erythrocytes, Millions/12 Hr.		
	D*	A†	D	A	D	A	B‡	D	A	B	D	A	B	D	A	B	D	A	B	D	A
										A. During Rheumatic Phase											
1	..	..	160	...	....	....	11.2	12.4	....	9,700	6,000	.....	0.46	0.10	....	0.050	0.100	.....	4.0	0.84	....
2	..	..	...	...	....	....	14.4	13.4	....	6,200	6,050	.....	....	....	....	.....	.....	.....	....	....	....
3	0	..	...	...	1.26	....	12.6	12.6	....	6,000	5,700	.....	0.42	0.46	....	0.273	0.117	0.087	0.58	0.053	0.39
4	..	..	...	...	....	....	11.8	11.8	....	6,400	5,700	.....	0.04	0.12	....	0.032	0.014	.....	0.256	0.256	....
5	..	..	...	...	1.6	....	10.8	12.2	....	8,350	4,500	.....	1.58	0.56	....	0.043	0.002	.....	1.5	0.389	....
6	0	..	160	...	0.52	....	14.0	12.2	....	7,200	6,000	.....	0.02	0.12	....	0	0.003	.....	1.1	0.285	....
7	0	..	156	140	0.92	....	15.0	15.2	....	9,800	4,600	.....	0.14	Trace	....	0.347	0.163	.....	0.12	0.315	....
8	0	..	166	...	1.0	....	13.4	11.5	....	7,500	6,800	.....	0.36	Trace	....	0.025	0.006	.....	5.5	0.690	....
										B. During Febrile Phase											
9	0	0	...	140	....	0.5	13.4	10.8	14.0	6,300	3,400	4,500	....	....	....	.....	.....	.....	....	....	....
10	0	0	...	164	....	....	12.8	10.0	12.0	6,700	4,500	5,700	0.40	....	0.09	0	.....	0	1.4	....	0.85
11	0	0	226	...	1.05	0.45	13.2	9.4	12.4	6,900	3,300	5,500	0.32	0.12	0.08	0.850	0.048	0.044	0.200	0.864	0.750
12	+	?	296	...	1.3	0.18	14.2	10.4	12.2	7,050	4,650	9,700	1.74	0.41	0.60	0.240	0.032	0.028	0.92	0.36	0.43
13	+	0	256	160	....	0.8	12.0	7.8	13.0	4,850	8,750	5,450	0.37	0.20	0.6	0.024	0.019	0.055	0.18	0.696	0.15

* D = during rheumatic or febrile phase. † A = after rheumatic or febrile phase. ‡ B = before hydralazine therapy was begun.

Most of the eight patients had been taking antihistaminics as part of their system of hydralazine treatment; in these the dosage of the antihistaminic (tripelennamine [Pyribenzamine] citrate) was increased from 200 mg. to 600 mg. daily, with the onset of arthralgia, which, however, it failed to control. Acetylsalicylic acid (aspirin) (3 to 6 gm. daily) gave relief to some but was ineffective in most. Ascorbic acid, nicotinic acid, isoniazid (isonicotinic acid hydrazide), nitrogen mustard, and hexamethonium chloride were given various patients in the hope of controlling the condition and maintaining hydralazine therapy; all were completely ineffective.

Cortisone and corticotropin (ACTH) gave symptomatic relief when they were given at the height of the rheumatic state. Steroidal therapy was continued in one patient over a period of four months. This patient had had a syndrome of malignant hypertension that responded favorably to hydralazine for seven months, during which her pressure averaged 160/90 mm. Hg. Discontinuance of therapy with the drug at the onset of the rheumatic illness resulted in a prompt rise of pressure to an average level of 230/130 mm. Hg; therefore, she was again given hydralazine, and the rheumatic state was suppressed successfully for four months, with 25 mg. of cortisone given four times daily. At the end of this time the patient's symptoms recurred, in spite of cortisone therapy.

The most effective means of causing the rheumatic phase to abate was to withdraw medication. Symptoms disappeared, on the average, within a week; one patient was completely relieved at the end of 24 hours and another not until 4 weeks. This last patient had continued using hydralazine for eight weeks while suffering from generalized joint pain and stiffness that was not relieved by aspirin. Hydralazine therapy was discontinued and another drug given over a period of 18 months, at the end of which hydralazine therapy was reinstituted and tolerated in a dose of 250 mg. daily with no return of joint pain. With this exception, all patients had recurrence of the rheumatic state when treatment was reinstituted; however, three have been able to take hydralazine at lower doses (150 to 300 mg. daily) while they also used aspirin as a means of controlling their residual recurrent discomfort.

The Febrile Phase.—The term "febrile phase" was used to describe the illness that supervened in five patients (tables 1, *B* and 2, *B*) and that, as will be shown, resembled acute systemic lupus erythematosus. The average duration of therapy in these patients before the onset of the rheumatic symptoms that preceded the febrile phase was longer than in those who had the rheumatic phase only; furthermore, these patients continued taking hydralazine after the onset of joint symptoms, three of them because the symptoms were relatively mild and two, whose distress was greater, by reason of their determined dispositions. Consequently, the average duration of treatment before the onset of the febrile phase was 17 months.

The initial rheumatic state of these patients was succeeded, after varying intervals, by a syndrome of temperature as high as 105 F, prostration, chest and abdominal pain, and physical and laboratory signs resembling those of acute systemic lupus erythematosus; in three patients polyserositis developed with pleural and pericardial effusions, one had extensive, nonspecific pneumonitis, and one had erythema of the hands and forearms. Details of each case are summarized in case reports below.

The outcome of the febrile illness was varied; in the patient whose major manifestation was erythema, the febrile illness subsided while hydralazine therapy was continued; the patient who manifested pneumonitis recovered after withdrawal of hydralazine and while she was being given isoniazid; of the three with polyserositis, one recovered after withdrawal of hydralazine, one responded to a course of corticotropin and cortisone, and the other remained on a maintenance steroidal program. As those with the rheumatic phase only, patients with the febrile illness did not show increased proteinuria, hematuria, or cylindruria. Arterial pressure, as compared to pretreatment control levels, was greatly decreased during the febrile illness and for some days thereafter.

REPORT OF CASES

Case 1.—A 46-year-old man (ninth patient, table 1, *B*) had been successfully treated for the malignant phase of essential hypertension with hydralazine, 800 mg. daily. For 18 months his diastolic blood pressure averaged 100 mm. Hg, as compared with pretreatment averages of 120 mm. Hg. The present illness began three weeks before he visited the outpatient department. After three days, he was treated with generalized ultraviolet light irradiation, which was followed in 24 hours by a blotchy erythema over the hands, forearms, neck, and face. His symptoms subsided, but the erythema persisted. He lost 10 lb. (2.3 kg.) in weight, and his blood pressure averaged 150/70 mm. Hg. He took medication throughout this time. On his visit as an outpatient, he appeared chronically ill with a temperature of 98 F, pulse rate of 96, and blood pressure of 148/88 mm. Hg; a blotchy erythema covered the dorsa of the hands and forearms, the forehead, and the neck. The heart was slightly enlarged on the left side. The spleen was palpable 3 cm. below the costal margin, as it had been three months previously. The blood hemoglobin level was 10.8 gm. per 100 cc. and the white blood cell count was 3,400 per cubic millimeter. The L. E. test was negative. The Tiselius protein pattern showed depression of the albumin fraction and elevation of the alpha and gamma globulin fraction (fig. 1). A biopsy specimen of the inflamed skin is shown in figure 2.

By a misunderstanding, hydralazine therapy was continued for 10 days, during which time erythema persisted without other symptoms. When the drug was withheld for three weeks the rash disappeared, the hemoglobin level rose to 13.3 gm. per 100 cc., the leukocyte count to 4,500, and the blood pressure to 170/96 mm. Hg. The drug was given again at a dosage of 200 mg. per day. Seven weeks later, the patient had slight discomfort of the interphalangeal joints of the hands. The serum protein pattern, however, returned nearly to normal. The patient now takes 100 mg. of hydralazine daily, without recurrence of any of his previous symptoms or signs.

Case 2.—A 60-year-old man (10th patient, table 1, *B*) took 800 mg. of hydralazine daily for 18 months because of severe essential hypertension with retinopathy. He felt well until the last three to four months of this time, when he had three episodes of upper respiratory tract infection; during the last six and a half weeks the interphalangeal joints became swollen, stiff, and painful. He was admitted to another hospital for study. He had fever, clinical and roentgenographic evidence of pleural and pericardial effusions, leukopenia, increased sedimentation rate, and anemia. Examinations of the peripheral blood to demonstrate the L. E. factor were negative, as were urine and sputum cultures, specific febrile agglutination tests, and tuberculin tests. The use of hydralazine was discontinued. The patient was given penicillin, chlortetracycline (aureomycin), and streptomycin without effect on fever or the course of the illness. Therapy with corticotropin was begun, and

within 48 hours he was afebrile, and the signs and symptoms of the disease began to disappear; use of corticotropin was soon discontinued. A few days later, the patient remained asymptomatic and began using hydralazine again on the day of his discharge from the hospital. When we saw him five weeks later, his only complaint was decreased endurance; he had taken 100 to 600 mg. of hydralazine daily without incident. The only residual findings were roentgenographic evidence of old pleural reaction and elevated gamma globulin level (fig. 1).

CASE 3.—This 38-year-old man (11th patient, table 1, *B*) responded favorably to hydralazine in doses of 800 mg. daily for the first five months and 600 mg. daily for the next six months. He noted the onset of pain and stiffness of fingers, wrists, elbows, shoulders, knees, and ankles and swelling of the interphalangeal joints of the hands; these findings were inconstant at first and then became persistent. Acetylsalicylic acid gave partial relief. The patient continued in this condition for two months, during which he also noted migratory pains in the muscles of the abdomen and chest. He became acutely ill two weeks before admission; he complained of pleurisy, malaise, and temperature to 104 F daily. Chlortetracycline gave no relief; use of hydralazine was continued until one day before admission. On admission, the man had the appearance of one who is both acutely and chronically ill. He had a temperature of 102 F, pulse rate of 120, respiration of 24 per minute, and blood pressure of 180/90 mm. Hg. The heart was enlarged to the left; a grade 2 systolic murmur and a pericardial friction rub were heard. The lower third of both lung fields was dull to percussion, with diminished fremitus and breath sounds. The proximal interphalangeal joints of both hands were swollen. The blood hemoglobin level was 9.4 gm. per 100 cc., the white blood cell count was 3,300 per cubic millimeter, serum polysaccharide 226 mg. per 100 cc., and erythrocyte sedimentation rate 1.45 mm. per minute. The chest roentgenogram showed evidences of pericardial and bilateral pleural effusion. The plasma L. E. test was negative, as was the tuberculin skin test. Pleural and pericardial fluids were sterile; the former had a specific gravity 1.018, with 2,100 lymphocytes per cubic millimeter. The electrophoretic analysis of serum proteins gave findings characteristic of this group of patients. Treatment was expectant only; the patient was maintained on a diet containing 0.5 gm. of sodium per day, and his discomforts were relieved with aspirin; over a period of three weeks, all signs of the illness disappeared. On the 23rd hospital day, he was given 25 mg. of hydralazine intramuscularly and palpitation and facial flush developed. On the following day, his morning temperature was 100.2 F, and his hands were stiff and sore but not swollen. Starting on the 25th hospital day, he was given increasing doses of hydralazine, first intramuscularly and then orally, until on the 34th day he was taking 600 mg. daily, which dose was continued for another 8 days; during this 17 day period of treatment he experienced arthralgias, pleuritic pains, and migratory myalgia, and his temperature ranged to 99.4 F or 100.6 F daily. The laboratory evidences of his former illness, which had subsided, did not recur during this time. The use of hydralazine was discontinued, however, because of the patient's discomfort; he was then given iproniazid and was discharged from hospital in good health. He has remained well.

CASE 4.—A 52-year-old man (12th patient, table 1, *B*) was given hydralazine for the control of severe essential hypertension with only a moderate success, so use of the drug was discontinued after an average daily dose of 500 mg. had been taken for 14 months. Treatment was reinstituted four months later, and the dose was rapidly increased to 800 mg. daily; because of lassitude and anorexia the dosage was further decreased, to 400 mg. daily, at which level it was kept for four months. During the last of these months, the patient began to experience pain and slight swelling of the wrists and interphalangeal joints and myalgia in the muscles of his legs. Two weeks later, malaise, substernal pain, a cough productive of mucoid sputum and a daily temperature range to 104 F developed. During the second week of this illness, the joint and muscle distress disappeared. Erythromycin and chlortetracycline gave no relief, and admission to the hospital was advised. Since the patient's blood pressure had fallen to normal levels, the use of hydralazine was discontinued for three days before admission on the 12th day of the severe illness. On admission, he seemed acutely ill, with temperature of 101.6 F, pulse rate of 100, and respirations 20 per minute. Arterial pressure was 148/100 mm. Hg. The fundi showed constriction of 1+ and sclerosis of 2+. The left border of cardiac dulness was 14 cm. from the midsternal line in the fifth intercostal space. A pericardial friction rub was heard. The lower third of both lung fields was dull to percussion posteriorly, with diminished breath sounds and a few, scattered, fine rales.

Chest x-ray showed evidences of pericardial and bilateral pleural fluid accumulations. The blood hemoglobin level was 11.0 gm. per 100 cc., white blood cell count 4,650 per cubic millimeter, sedimentation rate 1.3 mm. per minute, and serum polysaccharide 200 mg. per 100 cc. The plasma L. E. test was negative, but sternal marrow showed changes suggestive of lupus erythematosus. Muscle biopsy (fig. 3) showed infiltration of the muscle and perivascular tissues with lymphocytes. Blood and pleural and pericardial fluids were sterile in culture. The protein pattern showed decreased albumin and increased alpha and gamma globulins. The patient's condition deteriorated during the first hospital week; his temperature persisted at levels of 102 and 103 F. He was given 200 mg. of cortisone in divided doses on the eighth hospital day, at the end of which time he was afebrile and subjectively much improved. He continued to receive 50 mg. of cortisone every four hours for the next three days. Cortisone dosage was then slowly decreased, and corticotropin was given in two 10 mg. doses daily for 10 days, at the end of which time cortisone therapy was stopped and corticotropin dosage was decreased by halves over two days and then discontinued. On the following day, the patient complained of pain in the left side of the chest and had a temperature range to 101.6 F. By the next day he was acutely ill, with a cough productive of bloody, mucoid sputum and with signs of pneumonia in the base of the left lung. Repeated smears and cultures of sputum yielded only Candida; L. E. cells were again found in sternal marrow. This illness did not respond to penicillin or erythromycin therapy, so that, after three days of fever, cortisone and corticotropin were given again. On the sixth day of this fever, when the cortisone dose was 600 mg. and the dose of corticotropin was 20 mg. daily, the temperature fell to normal and the pneumonia began to clear. Cortisone dosage was gradually decreased to 100 mg. daily and corticotropin was decreased to 10 mg. daily over the succeeding days, during which progressively fewer clinical and laboratory evidences of the patient's illness were found and his blood pressure rose from an average level of 147/103 mm. Hg to levels of 180/120 mm. Hg and above. Slight fever and severe night sweats recurred whenever attempts were made to decrease the hormone dosage, so that this treatment was continued.

CASE 5.—A 36-year-old Negro woman (13th patient, table 1, *B*) had been satisfactorily treated with pyrogens over a six month period because of essential hypertension in the malignant phase. She was then maintained with 600 mg. of hydralazine daily for 17 months, with blood pressure at nearly normal levels. During the 13th month of this treatment, she noted pain and stiffness of her fingers and wrists; this was at first intermittent and responsive to acetylsalicylic acid but became progressively constant, irresponsive, and severer. During the four months that preceded her admission, she suffered severe recurrent upper respiratory tract distress that seemed to be infectious; she also observed an intermittent erythema and pruritus over the trunk. During the month before admission, she had cough, fever, and pleuritic pain and had lost 10 lb. (4.5 kg.) of weight. On admission, she seemed both acutely and chronically ill, with a temperature of 101.6 F, pulse rate of 124, respirations of 24, and blood pressure of 100/88 mm. Hg. The nasal mucosa was red and swollen, and patches of medium moist rales were scattered over both lung fields. The chest roentgenogram showed a diffuse, finely mottled infiltration of the lung parenchyma; there was no pleural fluid. Blood hemoglobin level was 7.8 gm. per 100 cc., white blood cell count 8,750 per cubic millimeter, serum poly-

saccharide 256 mg. per 100 cc., erythrocyte sedimentation rate 0.8 mm. per minute, and L. E. test (patient's plasma with dog marrow) positive. The Tiselius protein pattern (fig. 1) showed depression of albumin, with elevations of alpha and gamma globulins. Searches for a bacterial origin of this disease were ineffective. Tuberculosis was particularly suspected because the patient reputedly had had this disease at the age of 14; however, six sputum smears and cultures and five gastric washings were negative; also negative were tests for cold, Brucella, and typhoid agglutinins. There were no evidences of histoplasmosis or Q fever, and repeated blood cultures were sterile.

The patient remained miserably ill for seven days, with cough, pleurisy, and temperature range to 103 F. On the eighth hospital day, isoniazid was given in doses of 200 mg. daily. Over the next two weeks the temperature slowly fell, the symptoms, including pain in the joints, disappeared, and the pulmonary lesions cleared. Blood transfusions raised the blood hemoglobin level to 10 gm. per 100 cc., and the electrophoretic pattern of serum proteins was restored toward normal. The plasma L. E. test became negative. The woman was discharged in comparatively good health, on the 39th hospital day. When she was seen five weeks later, her blood pressure had risen to an average of 175/116 mm. Hg, she had regained her lost weight, the x-ray evidences of pulmonary disease had completely cleared, the blood hemoglobin level was 13.0 gm. per 100 cc., and the serum protein pattern was more nearly normal.

COMMENT

The data show that the use of relatively large doses of hydralazine for long periods of time by patients with essential hypertension elicits in some a syndrome, mild or severe, which variously simulates rheumatoid arthritis and acute systemic lupus erythematosus. The milder phase, characterized by joint and muscle distress, is associated with changes in plasma proteins that resemble those of the severe phase, which, in turn, resemble the changes found in systemic lupus erythematosus. The occurrence of fever in one patient, and of leukopenia in another with the milder rheumatic syndrome, probably represents transition into the severer phase of the illness.

The simulation of lupus erythematosus by the hydralazine syndrome is not complete. Thus, the plasma L. E. test was consistently negative in patients with the milder form of the disease, whereas it is usually positive in patients with acute systemic lupus erythematosus, who exhibit only the faint symptoms of that disease. Even in the severer phase, only one patient of five showed a positive plasma L. E. test and one other had L. E. cells and rosets in the bone marrow; both might have been expected to occur more uniformly in patients with acute systemic lupus erythematous of comparable clinical severity. In this connection, it is perhaps noteworthy that one patient, not reported on in this group, who was receiving treatment with hydralazine was found to have a positive plasma L. E. test, without any other signs or symptoms of the syndrome.

The distribution of the cases also differs from that of lupus erythematosus; four of the five patients were men, whose ages ranged from 38 to 60 years, and the other was a Negro woman. Another dissimilarity is the absence of increased proteinuria and cylindruria in the severe phase of the illness; such are common in lupus erythematosus, but, in our patients, the proteinuria and cylindruria attributable to nephrosclerosis tended to subside during the illness. Furthermore, the pneumonic processes experienced by two of the patients are not common in acute systemic lupus erythematosus; these seemed rather to resemble the pneumonia that occurs in rheumatic fever. The course of the illness is also different; remission occurred spontaneously in three of five patients with the severe form of the syndrome and in seven of eight with the rheumatic phase. The remission secured in two patients with severe disease by cortisone and corticotropin might be an aspect of similarity were it not that these drugs are similarly effective in a variety of mesenchymal diseases other than systemic lupus erythematosus.

In brief, hydralazine can, under appropriate conditions, elicit a state in the patient that simulates many aspects of acute systemic lupus erythematosus but that is evidently a distinct, although probably a related, process. The differences are sufficient to permit the conclusion that what has occurred is something other than an "unmasking" of latent systemic lupus erythematosus.

The precise classification of the syndrome induced by hydralazine, therefore, must remain uncertain. The most that can be said is that it falls within the group of varied diseases that Osler classified as the "erythema group." Periarteritis has been singled out of this group as a state that, in some instances, is attributable to hypersensitivity, and Rich [9] has suggested that others, notably lupus erythematosus and rheumatic fever, have a similar origin. The question thus arises as to whether the syndrome we describe is a manifestation of hypersensivity to hydralazine. Hypersensitivity is a tempting and facile explanation of any process that follows the use of a drug. Furthermore, hypersensitivity to penicillin sometimes elicits a positive L. E. test.[10]

The demonstration that this syndrome is a hypersensitivity to hydralazine is far from complete. It developed in patients without noteworthy evidences of an allergic diathesis; while some patients experienced recurrence of their symptoms on taking hydralazine after a symptom-free interval during which use of the drug had been discontinued, others did not, and some continued to take the drug, usually in smaller doses, without recurrence. In two patients the process continued after the use of the drug was stopped. These data suggest that hypersensitivity, as it is usually defined, does not account for the syndrome.

Rather, the syndrome develops in patients who have taken the drug for long periods and in doses large in comparison to those in common use. The severe form of the disease occurred only in patients who, after the milder phase of the syndrome had developed, persisted in taking the drug for weeks or months thereafter. These facts would be consistent with the view that hydralazine may in some way exhaust, impair, or change some aspect of tissue metabolism, in a purely quantitative way and by a mechanism quite distinct from that of hypersensitivity. Obviously, this is only opinion. An antigen may form from some of the hydralazine metabolite only when the dosage is such that the drug might saturate the tissues; alternatively, an antigen may form to which most persons are readily desensitized. Without evidence, it is futile to pursue this point; however, as we suggested

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above, a searching analysis of the mechanism that underlie this condition may bear on the pathogenesis of systemic lupus erythematosus.

SUMMARY AND CONCLUSIONS

In 13 of 139 patients under prolonged treatment with hydralazine hydrochloride (Apresoline) in relatively large doses, a syndrome supervened, which, in its milder phase, resembled early rheumatoid arthritis and, in its severer form, simulated aspects of acute systemic lupus erythematosus. The process usually disappeared spontaneously on withdrawal of therapy with the drug or on reduction in dosage. The severe form of the illness was controlled with cortisone and corticotropin (ACTH) in two instances, and one of these patients continues to receive maintenance steroidal therapy. The mechanism of the syndrome is obscure. While it may represent a variant type of hypersensitivity state, the quantitative aspects of data are consistent with the view that it is a toxic response to the drug as such.

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MODE OF ACTION AND EFFECTS ON TISSUES OF LONG-ACTING LOCAL ANESTHETICS

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and
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The search for satisfactory long-lasting local anesthetics for nerve blocking continues. The advent of each new drug or preparation appears to be a step toward a goal that has not yet been attained. A recently introduced and apparently a prematurely acclaimed preparation known as Efocaine has aroused our interest. Efocaine contains procaine base (1%), butyl-*p*-aminobenzoate (Butesin) (5%), and procaine hydrochloride (0.25%) in a mixture of polyethylene glycol (2%), propylene glycol (78%), and water (20%). Butyl-*p*-aminobenzoate is insoluble in water (1 gm. dissolves in 7 liters of water at 20 C) but soluble in organic solvents. Contact with an aqueous medium causes the procaine base and butyl-*p*-aminobenzoate to precipitate. Presumably the drugs are slowly absorbed when injected perineurally, and a long-lasting anesthetic effect is obtained. The possibility of depositing crystalline substances in the tissues on contact with water and a subsequent foreign body reaction has not been emphasized. Some have reported success with this preparation.[1] In our experience the long-lasting effect was not always obtained. Pain and soreness at the site of injection have been the rule rather than the exception. Symptoms of local inflammatory reactions have been frequent after its use. Preliminary reports state that Efocaine causes no local damage to tissues.[1a] The intense pain experienced after injection raises the question as to whether or not these findings are correct. The following case report is typical of the effects we have noted in the majority of instances in which we have used the substance.

REPORT OF A CASE

A right stellate ganglion block was performed on a 55-year-old white man for causalgia in the right forearm. The anterior approach was employed. The block was performed first with 5 cc. of 2% lidocaine (Xylocaine). A Horner's syndrome appeared, indicating the block was successful. Then 4 cc. of Efocaine was injected slowly. No pain or burning were felt at this time. One and one-half hours later the Horner's syndrome had disappeared. The patient experienced some relief of his pain that day. The next morning he complained bitterly of soreness in the right supraclavicular fossa in the region of the seventh cervical vertebrae. Some edema was present over a localized area several centimeters in diameter. The area was tender to palpation but not fluctuant. The pain in the arm for which the block had been performed had returned but was overshadowed by that present at the site of injection. There was no elevation of temperature. After three days the soreness subsided but no relief was obtained from the pain in the arm.

We have employed the substance for caudal block in terminal cases of carcinoma of the cervix and bladder. The results were disappointing. Unfortunately, postmortem examinations were not done. Others have noted the local soreness we have described. Moore and his associates [2] have collected five cases at the Masonic Clinic in Seattle of transverse myelitis following paravertebral injection of the drug. Davis [3] has noted neuritis following its use for intercostal nerve blocking at the University of North Carolina. Stephen and his associates [4] at Duke University have noted the same local soreness we describe as well as neuritis. Personal communications from other clinicians too numerous to list here reporting similar experiences have come to our attention.

In view of these facts we felt that further investigation of the local effects of this preparation was in order and that a comparison of the effects with those caused by other currently available substances for long-lasting anesthesia would be desirable. Few data are available on the histological changes induced by most of the so-called long-lasting local anesthetics.

Some of the currently employed preparations for long-lasting anesthesia are oily solutions of local anesthetic drugs. Many contain phenol or benzyl alcohol in addition to the local anesthetic drug. Ample studies have been

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Read before the Section on Anesthesiology at the 102nd Annual Meeting of the American Medical Association, New York, June 2, 1953.

This study was supported in part from a grant by E. Fougera and Company, New York.

1. (*a*) Weinberg, T.: Study of Effects of Efocaine upon Nerves, Muscle, Skin and Subcutaneous Tissue: Fougera Scientific Research Bull. no. 2, 1952. (*b*) Iason, A. H., and Shaftel, H. E.: New Approach to Problem of Postoperative Pain, Am. J. Surg. **83**: 549, 1952. (*c*) Ansbro, F. P., and others: Development of Efocaine: New Approach to Prolonged Local Anesthesia, Anesthesiology **13**: 306, 1952.
2. Moore, D. C.: Personal communication to the authors.
3. Davis, D. A.: Personal communication to the authors.
4. Stephen, R. C.: Personal communication to the authors.

made of the effects of these solutions on tissue. Studies by most workers indicate that their effectiveness is due to a destruction rather than to functional alteration of the nerve fibers. Duncan and Jarvis [5] have found that the benzyl alcohol in these solutions, particularly when used in concentrations over 10%, is responsible for their effect. Nonoily substances commonly used include absolute alcohol, phenol (6% aqueous solution), ammonium sulfate, benzyl alcohol in water, and monobromosalicylic alcohol (Bromsalizol) in propylene glycol. Uniform comparative studies would not be superfluous.

Fig. 1.—Degeneration and necrosis of the muscle 48 hours after injection of Efocaine.

The histological changes caused by intraneural alcohol injections have been described, but some disagreement exists between workers. Penman and Smith [6] report a complete destruction of nerves that persists for three and one-half months after injection. On the other hand Labat [7] reported no destruction after injection of 0.2 cc. of 95% alcohol intraneurally, even though total paralysis of the area supplied by the nerve was present. Mandl [8] reported necrosis of sympathetic ganglions 24 hours after injection of phenol, which was followed by regeneration after 75 days. Rabinovici [9] reported complete destruction of sympathetic ganglions by both phenol and procaine after intraganglionic injection. The results with phenol are as one would expect, but those due to procaine are surprising and questionable. Histological studies after the use of Dolamine (a mixture of ammonium sulfate, 0.75%, and benzyl alcohol, 0.75%) are not available. Data on the intraneural injection of aqueous solutions of procaine hydrochloride are also lacking. Minimal tissue changes after intramuscular and subcutaneous injections of procaine have been reported by deVincentiis and Meeker.[10] Vasodilatation, edema, and diapedesis of red blood cells were the commonest findings when a 1% solution of procaine hydrochloride combined with epinephrine was used.

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6. Penman, J., and Smith, M. D.: Degeneration of Primary and Secondary Sensory Neurones After Trigeminal Injection, J. Neurol., Neurosurg. & Psychiat. **13**: 36, 1950.

7. Labat, G.: Action of Alcohol on Living Nerve: Experimental and Clinical Considerations, Anesth. & Analg. **12**: 190, 1933.

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9. Rabinovici, N.: Anatomic Changes Produced by Novocaine and Phenol Infiltration in Sympathetic Ganglia, Surgery **31**: 877, 1952.

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MATERIALS AND METHODS OF STUDY

Obviously a study of this sort can only be done on animals. Rats three to six months old, weighing 200 to 300 gm., were used for most of the study. The animals were anesthetized with ether while the preparation being studied was injected. In order to note the effects on soft tissues, 0.1 to 0.2 cc. of each preparation or solution was injected into the muscle of the thigh or foreleg of the rat. Studies were also made by injecting the sciatic nerve perineurally, intraneurally, and both intraneurally and perineurally. For the perineural injection 0.10 cc. was used, and for the intraneural injection 0.05 cc. or less were used. The intraneural injections were made after exposure of the nerve by surgical dissection. A 27 gage ⅜ in. (0.96 cm.) needle was inserted at an acute angle to avoid trauma to the nerve. India ink was added to certain of the preparations to facilitate identification of the injected area for dissection. In all, 104 animals were used. When the effects on soft parts alone were studied, the forelegs were used. When both nerve and soft parts

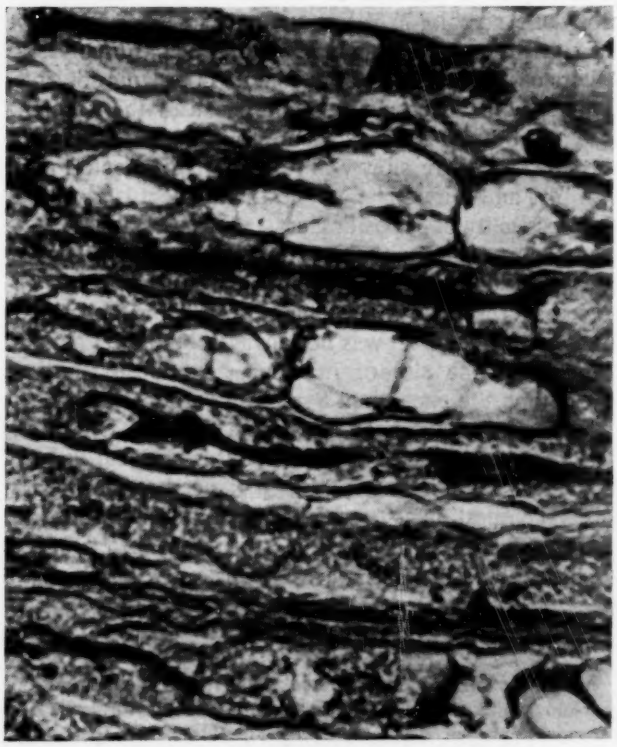

Fig. 2.—Coagulation necrosis of the nerve fibers 48 hours after injection of Efocaine into and around the nerve.

were studied, the thighs were used. Control studies were first made to note effects of isotonic sodium chloride solution and by introduction of the needle without any chemical agent. The animals were killed after 1, 2, 4, 7, 10, 14, 21, 30, and 68 days. None died from intercurrent infection; none had wound infections. Immediately after the animals were killed, the tissue was dissected and fixed in

Fig. 3.—Extreme dissociation in the nerve fibers 11 days after intraneural injection of Efocaine.

5% formaldehyde (Formalin). The majority of the sections were stained with hematoxylin and eosin. Special pains were taken to obtain nerve sections as strictly longitudinal as possible. To rule out the possibility that the results were due to species differences, injections were made in a few dogs. The results were identical, so the studies in these animals were limited.

RESULTS

Changes in Soft Parts.—Sections made two days after the intramuscular injection of 2% procaine hydrochloride showed no significant changes in perineural tissues and muscle. The ink was absorbed by phagocytes. Sections made a similar period after injection of Efocaine revealed degeneration and necrosis of the muscle bundle. There was a marked infiltration of lymphocytes and macrophages into the muscle (fig. 1). Sections made 10 days after intramuscular injection of Efocaine showed typical multinucleated regenerating muscle cells. Newly formed capillaries and fibroblasts were present that indicated an active regenerative process. By the 12th day most of the necrotic debris was removed, and regeneration was almost complete. Similar changes were caused by 6% phenol, alcohol, polyethylene glycol and propylene glycol mixtures, and polyethylene glycol (molecular weight 300). Muscle regeneration was present after seven days when phenol and alcohol were used. This was almost complete after 21 days. No degeneration or necrosis was observed in the muscle bundles of the controls after injection of isotonic sodium chloride solution, of 2% lidocaine, of Dolamine, or of 5% and 7% ammonium sulfate.

CHANGES IN THE NERVES

Two days after the intraneural injection of normal saline solution and India ink, no evidence of destruction was present even though considerable ink was present within the nerve. In contrast, after a similar period, perineural injection of Efocaine (fig. 2) caused coagulation necrosis of the nerve fibers. Bands of dead axis cylinders and an obvious absence of Schwann cells were noted, which indicates that no inflammatory or reparative process had yet occurred. The myelin sheaths had deteriorated into detritus, and nerve fibers had enormous vacuoles. Engorgement of the capillaries, diapedesis of red blood cells, and infiltration of lymphocytes were also noted.

Seven days after the perineural injection of Efocaine, vacuolization was pronounced and phagocytes and fibroblasts could be seen. The myelin appeared as globules that stained with eosin. The bands lost their prominence. Eleven days after the intraneural injection of Efocaine (fig. 3) extreme dissociation in the nerve fibers was noted. The neurilemma sheaths were empty, and a great increase of the number of Schwann cells was apparent. A coagulation necrosis of the fibers in the center of the nerve and infiltration of lymphocytes were noted. Between

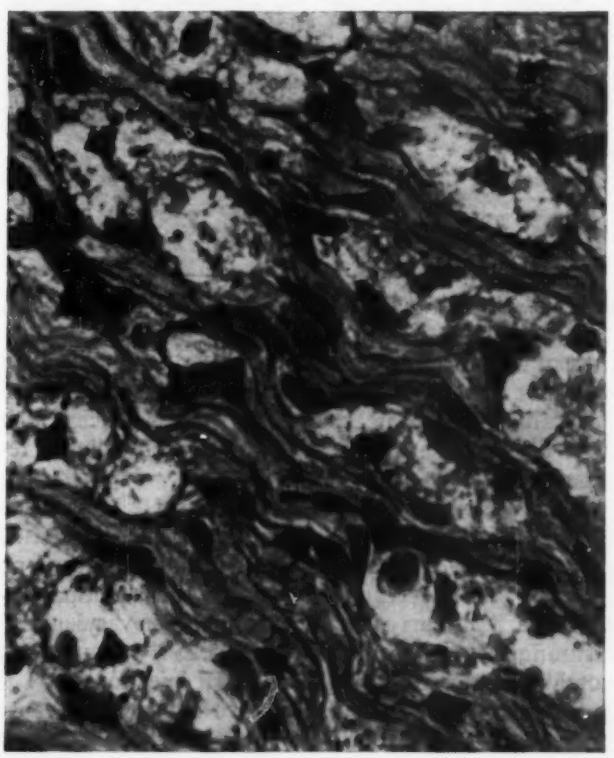

Fig. 4.—Regeneration of axis cylinders 68 days after intraneural injection of Efocaine.

the 14th and 60th day, the neurilemma sheaths were prepared for the ingrowth of regenerating axis cylinders. Sixty-eight days after the intraneural injection of Efocaine (fig. 4), regeneration of axis cylinders was noted. Considerable detritus of myelin was still present as well as an increase of the number of Schwann cells. Both lymphocytes and phagocytes were scattered throughout.

The propylene glycol and polyethylene glycol mixture (solvent for Efocaine) alone, and mixed with 5% butyl-*p*-aminobenzoate, caused muscle and nerve changes identical to the changes caused by Efocaine. Polyethylene glycol (molecular weight 300) caused similar changes.

The nerve destruction caused by phenol was extreme. Twenty-four hours after intraneural injection, pronounced band formation was noted (fig. 5). Phagocytosis of the ink particles had not occurred as yet. The Schwann cells were absent. A coagulation necrosis was

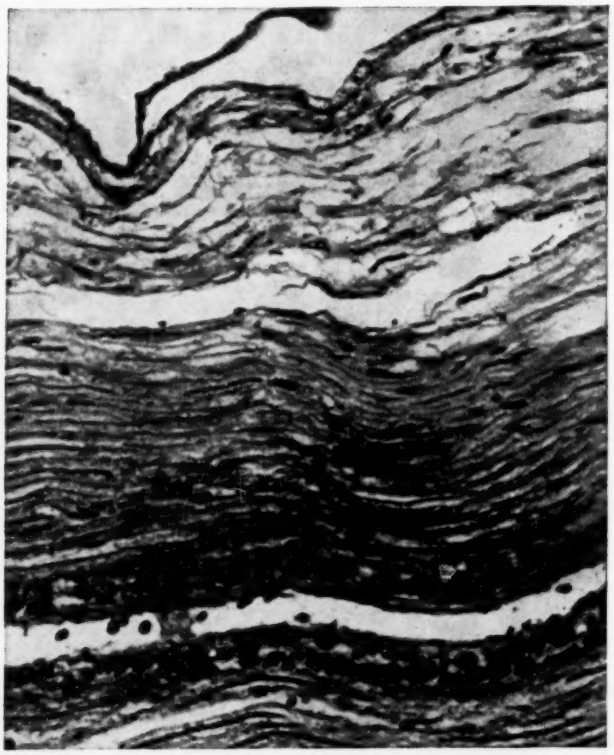

Fig. 5.—Pronounced band formation 24 hours after injection of 6% phenol.

present with no signs of macrophages or lymphocytes. In a similar fashion intraneurally injected alcohol caused qualitatively the same changes as phenol, except that after 68 days there were no signs of axis cylinder regeneration.

In contrast the intraneural injection of 2% procaine hydrochloride and 2% lidocaine hydrochloride caused no notable changes in the nerves. Dolamine caused no changes. After seven days the nerve had a normal appearance. Solutions of ammonium sulfate in varying concentrations (1.75%, 3.5%, and 5.25%) caused no notable damage following intraneural injection.

Handling or stretching the nerve appeared to cause no damage. This confirms the findings of Denny-Brown and Doherty,[11] who reported that a nerve must be stretched 40% to 100% of its length for damage to occur.

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COMMENT

It is difficult to correlate alterations in nerve function with morphological changes. The fact that function returns before regeneration is complete or that sensory changes may be obtained without any injury to nerves (as with ammonium sulfate) is not easily explained. One can only conclude that long-lasting local anesthetics, as in the case of the oily local anesthetic solutions, act by nerve destruction and that the changes induced are similar to those noted when a nerve is sectioned.

Degenerative changes in the nerves after these substances were injected are as intense and complete after 24 hours as those that occur 96 to 144 hours after nerve section. Gutmann and Holubar [12] were able to detect the onset of Wallerian degeneration by means of polarized light after 24 hours in sectioned nerve. The usual histological methods do not reveal changes before 40 hours, and by 60 hours only mild changes are noted. The characteristic changes are noted after 80 to 168 hours have elapsed. Swank [13] estimates the time for full development of Wallerian degeneration after nerve section to be six to seven days. It is noteworthy that, in the studies using phenol, alcohol, Efocaine, the polyethylene glycol, and the propylene glycol and polyethylene glycol mixture, the changes ordinarily requiring a week to appear after nerve section are fully developed within 24 hours. These findings are identical to those recorded by Holbrook and Pilcher [14] following the injection of calcium penicillin intraneurally.

SUMMARY AND CONCLUSIONS

Neuritis and local irritation have been noted following the clinical use of Efocaine, a recently introduced proprietary preparation for long-lasting anesthesia. Efocaine is a solution of procaine base (1%), butyl-*p*-aminobenzoate (Butesin) (5%), and procaine hydrochloride in a mixture of polyethylene glycol (2%) and propylene glycol (78%). The effects of various currently used long-lasting anesthetic substances injected intraneurally and perineurally on nerve and muscle tissue were studied histologically in experimental animals. Comparisons were made with results of injections of isotonic sodium chloride solution in controls. The saline solution caused no damage to either muscle or nerve tissue. Two per cent lidocaine hydrochloride (Xylocaine), 2% procaine hydrochloride, Dolamine (a mixture of ammonium sulfate, 0.75%, benzyl alcohol, 0.75%, and aqueous ammonium sulfate) caused no damage following intramuscular injection and transient changes on intraneural injection.

Efocaine, the vehicle used to prepare Efocaine, 5% butyl-*p*-aminobenzoate dissolved in the vehicle, polyethylene glycol (molecular weight 300), absolute ethyl alcohol, and 6% phenol destroyed both muscle and nerve tissues. After combined perineural and intraneural injection the changes are identical to those occurring after a nerve is sectioned but occur more rapidly. Regeneration of the nerves began at variable times but usually after 60 days after the use of all drugs studied except ethyl alcohol. Alcohol, phenol, Efocaine, and the vehicle in Efocaine cause anesthesia by nerve destruction rather than by blockade due to their anesthetic effects.

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DUPUYTREN'S DISEASE OF THE FOOT

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Fibromatosis of the palmar fascia, or Dupuytren's contracture, has been the subject of many exhaustive studies, and much has been written concerning its etiology, pathology, and treatment. In most of these studies, reference has been made to the fact that there is occasionally involvement of the plantar fascia by a similar process. Since the involvement of the plantar aponeurosis is rarely symptomatic, it has been considered relatively unimportant. Recently, however, in separate reports, Skoog,[1] Luck,[2] and Pickren and co-workers [3] have shown that the lesion in the foot is a distinct clinical entity, with characteristic gross and microscopic anatomy. They have demonstrated that the lesion occurs more frequently than is generally recognized and that important problems in differential diagnosis may arise unless this distinct clinical entity is well known. In this paper, the term disease is used instead of contracture because, in the foot, contractures are rare since extension of the fascia to the phalanges is either absent or insignificant.

CHARACTERISTICS

In the foot, the lesion is characterized by nodule formation, medially, near the highest point of the longitudinal arch (fig. 1). Contractures are rare. Involvement of the plantar aponeurosis may be present without involvement of the palmar aponeurosis, or the lesion may be limited to one foot. Microscopic study demonstrates that the nodules consist of masses of well-differentiated, proliferating fibrocytes. They arise within the plantar fascia and usually bulge toward the subcutaneous tissue but occasionally toward the deep structures of the foot. Such nodules may arise anywhere in the plantar aponeurosis. Because of the tissue changes discussed, the lesion has been called fibromatosis of the plantar fascia. It is unfortunate that, because of local recurrences of these very cellular fibrous tumors, they have been overdiagnosed and overtreated as fibrosarcoma. It is well established that this is a benign lesion that is adequately treated by resection of the entire plantar fascia.

We have recently treated six patients with fibromatosis of the plantar aponeurosis. It is felt that the need for a more widespread awareness of the problems of recognition, diagnosis, and treatment warrant a brief report of these cases. In addition, we would like to discuss further the histopathology.

REPORT OF CASES

CASE 1.—A 72-year-old man was admitted to the hospital complaining of tender nodules in both feet. The nodule in the right foot had been present for 12 years and the one in the left foot for 8 years. For two years, he had noted the gradual development of a nodule in the right palm. The lesion in the palm was asymptomatic, but those in the feet were painful when bearing weight. Examination revealed early changes of fibromatosis in each hand and the characteristic tumor masses on the medial border of each foot (fig. 1). The entire left plantar fascia was excised through an incision extending from the first metatarsal head to the os calcis on the medial border of the foot. When the fascia was exposed, there were two nodules in the medial portion that bulged toward the subcutaneous tissue (fig. 2). The pathologist's report was as follows: "Section shows a portion of fascia with several adjoining focal areas of fibroblastic proliferation of the type seen in Dupuytren's contracture" (fig. 3).

The postoperative course was uneventful. The patient became ambulant with no pain in the left foot. At a later date, through a similar incision, the right plantar fascia was removed. The tumor mass on the right side was found arising within the plantar aponeurosis and bulged toward the deep structures of the foot. It was not encapsulated, and there was no evidence of infiltration of surrounding fat, muscles, nerves, or vessels. The pathologist's report stated: "The lesion noted on gross examination represents a cluster of several more or less discrete nodules that are invested and united by fibrohyaline connective tissue containing scattered dilated capillaries. The nodules proper are highly cellular and are composed of parallel bundles of closely packed fibroblasts of quite uniform morphology. The diagnosis is plantar fascia, Dupuytren's contracture." The wound healed, and the patient became ambulant with no complaints. One year later, there was no evidence of recurrence in either foot.

This patient's case illustrates the typical clinical picture and classic gross and microscopic appearance of symptomatic Dupuytren's disease in the foot. Since there was involvement of all four extremities, the clinical entity was easily recognized. It should be emphasized, however, that lesions were present in the feet long before there was recognizable disease in the hands.

CASE 2.—A 26-year-old man was admitted to the hospital complaining of painful nodules on the plantar surface of the right foot. When he was 18 years old, soon after induction into the Army, he noted the development of such nodules in both feet. They were excised, but, because of recurrences, additional nodules were removed one year later. The disease was then diagnosed as multiple neurofibromas of the plantar surface of the feet. Five years later, one nodule was removed from the right foot for biopsy. The pathologist's report was as follows: "The section contains several pieces of dense fibrous connective tissue that have the appearance of fascia. Among the fibrous strands of the fascia, there is new formed dense connective tissue in which there are spindle-shaped parallel nuclei. There is no evidence of inflammation or malignancy. The histological picture is most like that of Dupuytren's contracture of the palmar fascia."

On another hospital admission, the same slides were reviewed by another pathologist who reported "dense fibrous tissue compatible with, but not pathognomonic of, neurofibromas." A consultant pathologist reported: "Cellular fascial fibroma (some call these low grade fibrosarcomas) in which local recurrences can surely be expected." On the basis of a clinical diagnosis of Dupuytren's disease of the foot, the entire left plantar fascia was excised. The pathologist's report was "recurrent fascial fibroma." Two years after the operation, the patient had no recurrences in the left foot and had no com-

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Read before the Section on Orthopedic Surgery at the 102nd Annual Meeting of the American Medical Association, New York, June 2, 1953.

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Mr. Earl Bartlett, medical photographer at the Dearborn Veterans Hospital, took the photographs used to illustrate the paper.

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plaints other than "numbness" caused by resection of the medial plantar nerve. On his last hospital admission, he complained of pain in the right foot and asked for the radical operation that gave relief in the left foot. The plantar fascia was exposed as in case 1. Multiple nodules were seen throughout the fascia, and the defect resulting from previous surgery

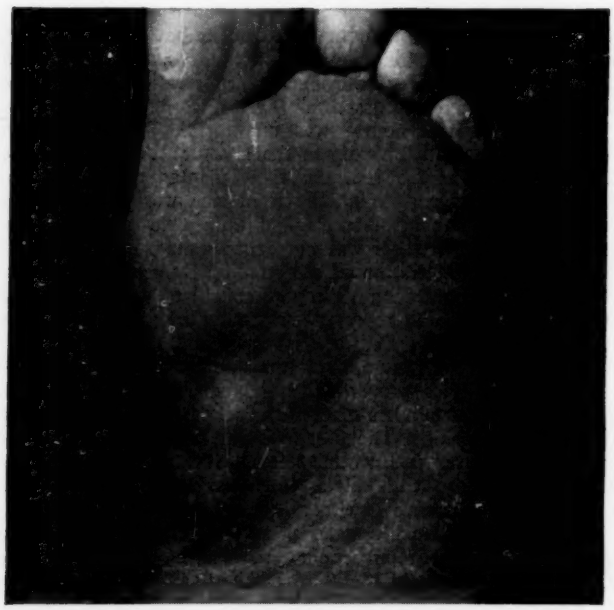

Fig. 1 (case 1).—The typical size and position of the tumor mass in Dupuytren's disease of the foot.

was plainly visible. The remaining fascia was excised. The pathologist's report stated: "The hard mass noted on gross examination consists of a conglomeration of small nodules composed of whorled bundles of fusiform cells resembling

Fig. 2 (case 1).—The tumor nodules arising from the medial portion of the plantar fascia.

fibroblasts. In the center of the nodule, these cells are closely packed and possess a very scant and somewhat poorly staining cytoplasm; toward the periphery, the connective tissue fibers become much courser, stain conspicuously with eosin, and appear partly hyalinized. This lesion is poorly delimited and appears to merge gradually with the adjoining fascia. The diagnosis is plantar fascia of the right foot, Dupuytren's contracture." The wound healed uneventfully, and he became ambulant and asymptomatic. He has since been lost to follow-up. His operations were performed in four different hospitals.

There was never any evidence of involvement of the palmar fascia. There was obviously much difference of opinion concerning the diagnosis. The impression of neurofibromatosis led several surgeons to the belief that surgical cure was not feasible. It is felt that calling these tumors recurrent fibromas or low-grade fibrosarcomas is both inaccurate and dangerous since it has resulted in unnecessary amputation. This patient's course illustrates that only complete excision of the plantar fascia prevents recurrence.

CASE 3.—A 27-year-old white man was admitted to the hospital for treatment of a tender nodule on the medial aspect of the left foot. Two years earlier, he had fractured the left tibia. As part of his fracture treatment, the left leg was placed in a walking plaster. When the cast was removed, the patient noted a callus on the medial border of the foot. Soon the callus disappeared, but it was replaced by a gradually enlarging mass beneath the skin, which was painful when bearing

Fig. 3.—Microscopic section showing great cellularity at the center of a nodule in Dupuytren's disease (hematoxylin and eosin stain; × 370).

weight. Four months after removal of the cast, the mass was excised through a small incision. The surgeon noted that it was a part of the plantar fascia and that its removal left a defect in the fascia. The pathologist's report was as follows: "The specimen consists of a hyperplastic scar rich in cells. This lesion should be completely excised." There was no evidence of disease in the other foot or in either palm. The patient was discharged for outpatient care and was readmitted nine months later for treatment of a recurrent mass.

Because of the pathologist's previous report, the patient was presented to the hospital tumor board where there was considerable discussion concerning the nature of this lesion. It was felt by some that the lesion represented a recurrence of a very cellular tumor previously suspected of malignant potentialities and that it should, therefore, be treated as a malignant lesion. The board finally recommended wide excision of the mass. At the time of operation, a large recurrent nodule in the plantar fascia was found, and the entire plantar aponeurosis was excised. The pathologist's report said: "The sections are similar to those seen previously in that the tissue again has the appearance of reactive fibroblastic hyperplasia. In addition to the increased cellularity, there are several normal appearing mitoses. This is felt to be compatible with clinical diagnosis of Dupuytren's contracture." Convalescence was uneventful. Two years later, there was no evidence of recurrence.

It is felt that this patient had classic Dupuytren's disease in one foot, without involvement of the other extremities. We have seen one other patient in whom the disease developed after the use of a walking plaster. Luck states that he has seen it several times, and Ledderhose [4] reported 50 cases in 1897. The presence of the callus when the plaster was removed and the subsequent development of the mass immediately beneath the callus lend support to the thought that trauma in some instances precipitates the disease.

Finally, from the discussion concerning the diagnosis in this case, it is obvious that an unnecessary amputation might have been suggested as proper treatment. We have recently seen a patient in the tumor clinic for follow-up examination who has a classic recurrence of Dupuytren's disease in one foot. He had two previous operations at another institution and was advised that, if there was any recurrence, his leg should be amputated.

COMMENT

Recently, Pickren, Smith, Stevenson, and Stout reviewed the world literature and, with 16 additional cases, discussed this disease thoroughly. They prefer to designate it as fibromatosis of the plantar fascia. They emphasized that between the years 1927 and 1949, only seven cases were seen at the Presbyterian Hospital in New York and that two of those were treated by amputation. During that same period, nine other patients were sent to their laboratory. In five of these, the lesions had been diagnosed as potential or actual fibrosarcoma. Their review contains a comprehensive discussion of the clinical features, pathology, etiological factors, diagnostic problems, and method of treatment.

It is our belief that this disease is commoner than is generally recognized. This report is based on a study of six patients who had symptomatic involvement of the plantar fascia. It is felt that the significant features of the disease are adequately illustrated by the cases already discussed. Patients who had symptomatic palmar involvement with minimal asymptomatic plantar disease have not been considered. It appears very important to emphasize that, whatever the underlying cause may be, this disease may involve any one or all four of the extremities in various combinations. While the degree of involvement may vary, the clinical picture is characteristic. In the feet, contractures are rare because, as mentioned before, extension of the fascia to the phalanges is either absent or insignificant. Tumor formation is typical.

The term Dupuytren's disease has been retained because it is felt that it describes, for the clinician, a definite benign disease diagnosed on the basis of clinical and gross and microscopic pathological characteristics. Overtreatment is then unlikely. There are other reasons for designating this condition as Dupuytren's disease. There is as yet no agreement as to etiological factors. Pickren and associates discussed many factors, came to no conclusion, and, while remarking on the wide variety of causes suggested, stated that "while any one of these many bizarre associations of maladies with fibromatosis of the palmar and plantar fascia must seem due purely to chance, one pauses to wonder if they may not play the part of a trigger mechanism in individuals who have a congenital susceptibility."

In the present series of six patients, there is no common etiological factor apparent. Histological study of excised plantar fascia, however, reveals uniformly present changes that seem to indicate the mechanism by which any causative factor produces the fibrous tumor.

In previous studies, the tumor has been considered the important lesion. In discussing the pathogenesis of Dupuytren's contracture in the hand, Luck has stated that the nodule is the essential lesion. In discussing the microscopic appearance of the lesion in the foot, Pickren and associates stated that "the normal broad, acellular collagen bands of the plantar fascia terminated at nodules of young fibroblasts and interdigitated with other bundles of highly cellular new tissue." Skoog reported that these nodules arise in areas in which the normal collagen bundles are broken. He believes that nodules arise from perivascular connective tissue in response to such degeneration. He has demonstrated iron pigment in the areas of degeneration. He believes that in the foot, whatever other causes might be involved, the lesion is more prominent on the medial side at the highest point of the arch because mechanical strain produces the greatest degree of fiber rupture. Ledderhose also reported that this is a degenerative disease.

In our own material, we have never seen the formation of nodules in an area of normal plantar fascia. It is felt that, in the areas of nodule formation, the fibrillation, fragmentation, hyalinization, and changes in staining reaction of collagen fibers indicate degenerative disease of connective tissue and that nodule formation represents a reactive hyperplasia. The presence of increased numbers of thick-walled small vessels and focal collections of round cells is considered part of the host response to a degenerative process. If it is felt that the underlying disease is degeneration of the plantar fascia, reactive nodules may develop in many areas, and only complete excision of the plantar fascia will prevent recurrence.

It has frequently been stated that, in many cases, unusual trauma has appeared to precipitate the disease, yet, because it is difficult to demonstrate that trauma plays an important role in the majority of patients, it is usually held that the history of trauma is incidental. If it is believed that degenerative change precedes tumor formation, then it seems rational that unusual trauma to normal fascia might produce the necessary degenerative process and, therefore, be the important etiological factor. It is conceivable also that many agents might change the palmar or plantar fascia so that degenerative change follows what is considered normal use. On the basis of the evidence available, one does not seem justified in excluding trauma as a cause of Dupuytren's disease or fibromatosis of the plantar fascia.

SUMMARY AND CONCLUSIONS

Fibromatosis of the plantar fascia or Dupuytren's disease is a distinct clinical entity that occurs more frequently than is generally recognized. It is suggested that the disease is a reactive fibrous hyperplasia following degenerative disease of the plantar fascia.

Unless the lesion is recognized as a clinical entity, benign in nature, the histological features associated with recurrences may suggest malignant disease and result in overtreatment. Only complete excision of the plantar fascia will prevent recurrence.

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LONG-TERM RESULTS IN CORTICOTROPIN-TREATED ULCERATIVE COLITIS

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The use of corticotropin in the treatment of idiopathic ulcerative colitis was first reported in 1950.[1] Since that time a number of investigators have observed a favorable immediate response to this form of therapy, particularly when the disease was of the acute fulminating variety and of short duration.[2] Our experience with the initial response of ulcerative colitis to corticotropin has been previously reported and corresponds closely to that of others.[3] In the majority of patients a prompt defervescence, reduced number of liquid stools, better appetite, weight gain, correction of anemia, and greater emotional stability followed when this hormone was added to the usual supportive measures. An improvement in the proctoscopic and roentgen appearance of the colon regularly showed a lag in comparison to symptomatic improvement. The original group of patients now have all been followed for over two years. The course of these and additional patients who have had prolonged observation following corticotropin therapy forms the basis of this report.

METHOD OF STUDY

We have now administered corticotropin to 40 patients with ulcerative colitis; 26 were men, 14 women. Nineteen were in the third decade, eight in the fourth, six in the fifth, three in the sixth, and four in the seventh. Seven patients were classified as acutely ill, 18 as severely ill, 14 as moderately, and 1 as mildly ill. Only five were having their first attack of ulcerative colitis; one had a history of the disease for 25 years and the rest for 3 to 10 years. Significant relapse had occurred in the majority every one to two years. All patients except one were treated in the hospital, and when the history was taken particular attention was paid to any facts suggesting previous or existing tuberculosis, diabetes, or peptic ulcer. Routinely a blood cell count, urinalysis, blood Wassermann test, blood sugar, stool and proctoscopic examination, and gastrointestinal and chest roentgen-ray study was performed.

Both the Armour [4] and Wilson preparations of adrenocorticotropin hormone were employed. Initially 20 mg. (Wilson) or 25 mg. (Armour) of corticotropin was administered intramuscularly every six hours until some clinical effect was demonstrable, which usually occurred during the first week. The dose was then gradually reduced according to the patients' response during two additional weeks. In many of the patients with mild or moderate disease only 20 mg. every 12 hours was sufficient to produce clinical improvement in approximately one week and permit reduced amounts to be given during the second and third weeks. When the corticotropin was given intravenously, according to the technique of Gordon, Kelsey, and Meyer,[5] 20 mg. was given in 500 cc. of 5% dextrose in water continuously for eight hours daily for one to two weeks. During the third week a reduced amount of the hormone was given intravenously or a tapering off dose intramuscularly according to the clinical response. We now prefer this dosage and method of administration to all others and have given it to half our patients originally and to all with delayed response. One patient had a satisfactory response with 10 mg. given intravenously daily for 10 days. Eosinophil counts were used originally to determine when the corticotropin was having an eosinopenic effect, but we observed that clinical response would frequently occur when the dose of corticotropin was too small to cause a fall in the eosinophil count. We therefore discontinued this test as a routine procedure and utilized the clinical response as the guide to dosage. In the majority the most effective dosage appeared to be 20 mg. given as a slow intravenous drip over an eight hour period daily, continued until a clinical response was manifested by a fall in fever, reduced stools, improved appetite, and increased sense of well-being. Whether given intravenously or intramuscularly, corticotropin therapy was rarely continued longer than three weeks.

In addition to hormone therapy all patients received the supportive measures ordinarily used in the treatment of ulcerative colitis. These included bed rest, sedatives, parenterally administered fluids, whole blood transfusions, antibiotics, and a high caloric, high protein diet. To maintain electrolyte and mineral balance, potassium chloride, 2.0 gm., and dicalcium phosphate, 2.0 to 4.0 gm., were administered orally each day. Testosterone propionate, 25 mg. intramuscularly daily, was given for its anabolic effect to three severely ill male patients for 10 to 14 days.

RESULTS

Of the 40 patients treated, 15 have been followed over two and one-half years, 10 over two years, 10 over one and one-half years, and 5 less than one year. The response

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Read before the Section on Gastroenterology and Proctology at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

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4. Some of the corticotropin (Armour) was supplied through Harley E. Claxton, M.D., director of medical research, the Armour Laboratories, Chicago.

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to the initial course of therapy under our supervision was classified as excellent in 8, good in 14, fair in 6, and poor in 2. The type of response did not correspond to the severity of the illness. Of the two patients showing a poor response, one was a 53-year-old man who had chronic disease of 25 years' standing and the other was a 19-year-old youth who was experiencing his first attack of ulcerative colitis, which was of the severe, fulminating variety. The patients who had a fair response, for the most part, had protracted, low-grade disease, and those in whom an excellent or good response occurred were noted to have widely spaced, severe exacerbations with periods of complete remission between.

Protoscopic study of patients in relapse revealed changes similar to those of the initial attack. Improvement in the colon frequently developed much more slowly than the subjective symptoms. A pronounced reduction in congestion, edema, and friability was usually not demonstrable until the second week of therapy and in some patients was delayed until the third or fourth week. Granularity seldom diminished; pseudopolyps were observed to decrease in size but not to disappear completely. Roentgenographic changes observed in the colon rarely showed much improvement and in the severely ill patient were at times progressive even though symptoms were in remission.

EARLY RELAPSE

Relapse following a course of hormone therapy has occurred in 16 of the 40 patients up to the present. In four this occurred early, within one to six weeks. In one of these patients this took place three times in fairly rapid succession; in the other three it occurred twice. Retreatment induced prompt remission of these relapses in all four patients, but it was maintained for a substantial period in only two; in one, continuous treatment with small doses of corticotropin was required, and in the fourth corticotropin therapy had to be discontinued because of the development of a severe acneform rash of the face and chest. The history of three of these patients follows.

CASE 1.—A 53-year-old pharmacist was admitted in a comatose state with a blood urea nitrogen of 110 mg. per 100 cc. He had had chronic recurrent diarrhea for 25 years and immediately prior to admission had been having 10 to 20 loose, watery stools per day. After correction of his electrolyte imbalance he was treated with cortisone, 50 mg. every 12 hours for two nonconsecutive two week periods, but an electrolyte imbalance gradually developed with hypokalemia and hypocalcemia. Cortisone therapy was therefore discontinued and symptomatic care administered. Three weeks after convalescence at home a severe exacerbation of diarrhea followed a period of great emotional stress. Anorexia, weight loss, and weakness soon developed. Because of financial difficulties the patient refused to reenter the hospital. Therefore, self-administered corticotropin, 25 mg. every six hours for two weeks and every 12 hours for one week, was prescribed, together with potassium chloride, 2.0 gm., and dicalcium phosphate, 4.0 gm. daily. This brought about a prompt improvement in appetite, weight, strength, and emotional outlook that persisted for about three weeks when an exacerbation of diarrhea followed a mild head cold. With the persistence of diarrhea the patient began to do poorly, and it was decided to repeat the course of corticotropin. This was again followed by remission, but, when corticotropin was completely withdrawn on this occasion, there was a gradual increase in stool frequency, anorexia, weight loss, and weakness. This finally became incapacitating and was only relieved by small doses (20 mg.) of corticotropin daily. Several attempts to withdraw the hormone completely, substituting distilled water injections or cortisone by mouth, all failed to keep this patient symptom-free. With only a few weeks' interruption he has used 20 mg. of corticotropin daily for 26 months. With this dosage he maintains his weight, feels well, and is able to work regularly, and his only symptom is occasional bouts of loose stools. Fasting blood sugar levels and urinalysis are normal. Repeat barium enema roentgen study at six month intervals has shown a gradual progression in contraction and loss of haustral marking of the colon and the development of inflammatory changes in the terminal ileum.

CASE 2.—A 19-year-old white youth noted occasional blood in bowel movements three months before admission. There were four to five loose stools daily containing mucus, pus, and blood, at the time of entering the hospital. Proctoscopy and barium enema roentgen study showed idiopathic ulcerative colitis involving the entire colon. The patient was inadvertently given for one week 40 mg. of corticotropin in 500 cc. of 5% dextrose in water intravenously over an eight hour period daily, instead of the 20 mg. we usually employ. During this week temperature of 103 to 104 F, severe bloody diarrhea with clots, and extreme abdominal pain and anorexia developed. The corticotropin therapy was therefore discontinued and supportive measures employed for another six weeks. During this time abdominal pain was so severe that perforation of the bowel was suspected several times. Surgical and medical consultants thought this patient should have ileostomy, but neither the patient nor his family would agree. He gradually improved sufficiently to go home, but two weeks later three subcutaneous abscesses developed, one on the thigh and one behind each ear that required incision, drainage, and antibiotics. This complication aggravated the diarrhea and the anorexia so much that the patient was readmitted. Corticotropin, 20 mg. every 12 hours, was given intramuscularly with a prompt decrease in fever and improvement in appetite and emotional state. The patient gained 8 lb. (3.6 kg.) in one week, but rather severe acne developed on the face and chest. Corticotropin therapy was discontinued, and the patient returned home, but diarrhea, abdominal pain, and anorexia recurred immediately. Cortisone, 25 mg. every 12 hours orally, was tried but seemed to aggravate the condition. This patient has had to be treated symptomatically since; his progress has been slow and complete remission has not been obtained to the present.

CASE 3.—A 24-year-old white man first noted bright red blood in his stool while in military service in Germany. After discharge and reenlistment abdominal cramps, loose or watery bloody stools, and weakness developed. Stool examination was reported to show trophozoites of Endameba histolytica. This led to intensive treatment with aureomycin and amebicides for about one month. During this time high fever, severe diarrhea, anorexia, weight loss, and anemia developed. Repeat proctoscopy indicated that these symptoms were secondary to ulcerative colitis and corticotropin, 20 mg. every six hours, was given intramuscularly for 14 days, with a gradually reduced dose over a period of eight weeks. As the dose was reduced to minimal levels and finally stopped, appetite and emotions became depressed, and stools increased. Retreatment with corticotropin was then instituted, and 20 mg. of corticotropin in 500 cc. of 5% dextrose in water given intravenously over an eight hour period daily was followed by prompt improvement. Treatment was continued for three weeks, and remission was sustained for 18 months.

LATE RELAPSE

Twelve patients suffered delayed relapses occurring 12 to 18 months after the initial hormone therapy. These were severe exacerbations usually associated with great emotional stress or upper respiratory infection. Retreatment of these patients with corticotropin brought about improvement, but in five this was less prompt and less complete than that obtained initially. They received corticotropin intravenously for one to three weeks, and

symptomatic treatment was continued in those who failed to respond completely. If symptoms persisted in spite of corticotropin therapy and supportive measures, cortisone, 25 mg. every 12 hours for one to three weeks, was given. This proved quite helpful in four of the five patients with refractory cases. One patient's condition was made worse by it. The following three cases are examples of delayed relapse showing different types of response to retreatment. The first case shows delayed relapse with satisfactory response.

CASE 4.—A 23-year-old white laborer had the first attack of acute fulminating ulcerative colitis 14 months previously that had been treated with corticotropin. There was complete remission in about 18 days. One month later he returned to hard labor, gained weight, and felt well. Relapse 14 months after the initial corticotropin therapy was preceded by a severe head cold, which was followed in three days by diarrhea of 5 to 10 liquid bloody bowel movements per day, anorexia, weakness, weight loss, and fever. Proctoscopy and roentgen study of the colon showed somewhat more advanced changes than had been observed the preceding year. Retreatment included 20 mg. of corticotropin intravenously daily for three weeks, bed rest, sedatives, transfusions, high caloric, high protein diet, and vitamins. Improvement occurred, but stools were still frequent and loose and appetite only fair at end of three weeks treatment. Corticotropin therapy was discontinued, and supportive measures alone were employed for 10 days. During this period a pronounced improvement in appetite, emotional state, and bowel function took place. This patient returned to heavy outdoor labor two weeks after discharge and has remained asymptomatic for four months.

The second case shows delayed relapse with unsatisfactory response to retreatment with corticotropin but subsequent improvement following cortisone therapy.

CASE 5.—A 23-year-old white clerk had ulcerative colitis for about three and one-half years. She had responded well to the first course of corticotropin therapy 20 months previously and had gained 35 lb. (15.9 kg.). After contracting a head cold, bloody diarrhea, fever, and abdominal pain developed, and she became very anxious. Admission to the hospital and three weeks of intravenous corticotropin therapy improved the outlook and appetite moderately. The temperature gradually fell to normal, but she continued to have four to five liquid to soft stools daily without gross blood. This response was much slower in developing and less complete than the one 20 months previously, nevertheless corticotropin therapy was discontinued. This patient was enthusiastic about her improved state while taking cortisone, and the drug was therefore given for three weeks and then stopped, even though the patient was reluctant to give it up. She has continued well up to the present, two months after all medication was withdrawn.

The third case shows delayed relapse, with unsatisfactory response to corticotropin as well as to cortisone.

A 61-year-old white woman had bowel dysfunction for four years, but it was diagnosed as ulcerative colitis only 13 months ago. Corticotropin was first administered at that time for three weeks. Response was excellent, with pain relief, return of normal bowel function, and improved appetite and emotional state. After remaining asymptomatic for one year, this patient contracted a severe upper respiratory infection and diarrhea developed, with 10 to 15 stools per day containing large amounts of mucus, pus, and blood. Proctoscopy and roentgen study revealed a progression of the old disease process in the colon. A repeat course of intravenous corticotropin therapy over a three week period produced some improvement in appetite and in reducing anxiety, but the stool and proctoscopic appearance of the rectum remained unchanged. The patient was discharged after three weeks' treatment for further convalescence at home. Her response was only fair, and she complained of considerable depression. Cortisone, 25 mg. every 12 hours, was then given for one week, but without benefit. Instead, anxiety developed to such a degree that the patient was afraid to remain at home alone because she contemplated suicide. She became emotionally stable when the cortisone was withdrawn.

COMMENT

The etiology of ulcerative colitis remains unknown, although infection, hypoprotinemia, allergy, hypermotility of the bowel, enzyme disturbance, and psychoneurosis are looked on as contributing factors. None of these theoretical factors, however, has been established, and consequently treatment remains empirical. Medically this consists of supportive measures such as bed rest, sedatives, a highly nutritious diet, parenterally administered fluids, blood transfusions, antibiotics, vaccines, vitamin supplements, and psychotherapy. Complications and intractability are usually considered indications for surgical intervention, which consists, preferably, of ileostomy and total colectomy. Since this is actually a systemic disease, at times showing widespread involvement of almost any system of the body, it is not surprising that nonspecific medical and surgical treatment [6] often fails to bring about complete cure, and a continued search for improved treatment is essential. Corticotropin has been shown to have a beneficial effect in a number of diseases of obscure origin in which widespread inflammatory reaction, polyarthritis, iritis, and involvement of mesenchymal tissue may be present.[7] The existence of some or all of these features in patients with ulcerative colitis led to the trial of corticotropin therapy in this disease. A number of investigators have now reported a favorable response, particularly in the acute fulminating form of colitis of short duration, but the mechanism whereby corticotropin produces this response is unknown. It has been suggested that the stimulating effect of corticotropin in the adrenal cortex produces cortisone-like steroids that inhibit the oversensitivity of mesenchymal tissue.[8] Whether such a reaction accounts for the reduction of the intense inflammatory bowel changes seen proctoscopically in these patients is still speculative. Alterations in enzyme systems, tissue permeability, and the mechanisms involving hyaluronidase may be postulated, but supporting evidence is not yet available. Among the many known effects of corticosteroids that might play a significant role in ulcerative colitis is an increase in gluconeogenesis with a sparing of carbohydrate to the body and the increased absorption and storage of fat.[8] On the other hand, there is an increased loss of nitrogen through the kidneys, and although fecal nitrogen loss is reduced the patient remains in negative nitrogen balance during corticotropin therapy.[9] It cannot be stated exactly how corticotropin works in ulcerative colitis, but clinical observation following its use shows in the majority of patients a sharp decline in fever, a reduction in the number of fluid bowel movements, improved appetite, gain in weight, correction of anemia, and a greatly improved emotional outlook.

6. Rogers, A. G., and Bargen, J. A.: Problems of a Patient with Ileac Stoma, J. A. M. A. **151**: 815 (March 7) 1953.

7. Thorn, G. W., and others: Medical Progress: Clinical Usefulness of ACTH and Cortisone, New England J. Med. **242**: 783, 824, and 865, 1950.

8. Boland, E. W.: Clinical Use of Cortisone, Hydrocortisone, and Corticotropin, J. A. M. A. **150**: 1281 (Nov. 29) 1952.

9. Kirsner, J. B., and Palmer, W. L.: Effect of Corticotropin (ACTH) in Chronic Ulcerative Colitis: Observations in Forty Patients, J. A. M. A. **147**: 541 (Oct. 6) 1951.

All our patients except one were treated in the hospital and have received, both initially and for relapses, corticotropin either intravenously or intramuscularly or both in gradually reduced dosage for a total treatment period of three weeks. In the early relapses retreatment with corticotropin brought about a response equally favorable to the initial one, but in 12 patients with delayed recurrences retreatment produced a slower and less effective response. We have preferred the use of corticotropin to cortisone both for initial treatment and for recurrence, but in five patients, whose response to corticotropin therapy was inadequate, cortisone was administered, 25 mg. orally twice daily for a period of one to three weeks. Four patients indicated that they felt stronger and had improved appetite and fewer stools; the fifth did not appear to be benefited. None of the patients in the entire group have had surgical treatment, and all but one have returned to their occupations. In the latter case surgery has been recommended, but neither the patient nor his family has been willing to accept it. At present he is ambulatory but still in a weakened condition.

We have observed no serious untoward reaction to the use of corticotropin, although acne occurred in one patient, moderate rounding of the face in three, and slight ankle edema in two. One patient showed considerable depression and anxiety after a course of corticotropin and cortisone therapy. All of these symptoms were relieved when hormone therapy was discontinued. The infrequency and mildness of side-reactions or complications in this group of patients is probably due to the small doses of corticotropin and the short period of administration, which rarely exceeded three weeks.

CONCLUSIONS

On the basis of our experience we consider corticotropin to be an effective therapeutic adjunct in the treatment of ulcerative colitis. It brings about changes similar to spontaneous remission but produces them more rapidly. It is not a cure, as is evidenced by the progress of the disease and the fact that relapse has occurred in approximately half of the treated patients and may still occur in the remainder. Early relapse is amenable to retreatment with corticotropin, but, when the relapse is delayed, response is less prompt and somewhat less complete. In the latter instances the addition of cortisone has been helpful.

2017 Delancey Pl. (3) (Dr. Wirts).

MEDICAL TECHNOLOGY AND ITS RELATION TO PHYSIOLOGY AND PATHOLOGY

CHAIRMAN'S ADDRESS

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In approaching a subject so vast it is tempting to spend more time than would be appropriate on the beginnings of the techniques, methods, and apparatus that form the tools of medical technology and how these tools and the ideas from which they came and to which they have led have influenced not only physiology and pathology but every other aspect of medicine, as well as our entire social and economic structure. It is also a temptation to discuss in greater detail than opportunity permits all the intimate relationships between medical technology in its broadest sense and physiology and pathology, two of the great fundamental divisions of medicine that utilize technical procedures more than any other. However, the scope of such a discussion would be so vast that it is necessary to limit it to a few of the most timely aspects.

If time permitted it would be easy to show that medical technology bears the same intimate relationship to physiology that it bears to pathology, or in fact to any other of the medical sciences. It is obvious that the same techniques must be utilized, whether the functions and processes of the organism are being studied and measured or the effects of disease on those same functions and processes observed.

The history of modern medicine is replete with milestones of technical progress, such as the development of the microscope, the discovery of the roentgen ray, and the identification of bacteria. Each of these technical milestones carries with it implications of many other techniques. Lowenhoek's little single lens microscope was the first anticipatory step toward our vast modern array of microscopes and microscopic techniques, not to mention an even vaster array of the uses of optics of all kinds and of the technical advances that they have made possible. The discovery of the bacterial origin of disease by Pasteur gave birth to a perfectly staggering array of technical methods and apparatus that have found their way into every corner of medical science and have transformed civilization beyond the wildest dreams of the little French chemist who started it all.

In contemplating such facts as these, it is often impossible to say whether this or that discovery has had more impact on the development of physiology or pathology. Also there is a constant flow back and forth between the techniques and concepts of disease and health.

Nor is it necessary to go back into the history of medicine to be confused, for it is often impossible to define the limits of what might be considered a physiological state so definitely that it is possible to say whether at another time or place it might not be considered evidence of disease. As an example, observations have been accumulating on the effects of the changes in intestinal flora produced by the antibiotics. These findings will lead to new concepts of the functions of the normal intestinal flora in health as well as in disease.

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Read before the Section on Pathology and Physiology at the 102nd Annual Meeting of the American Medical Association, New York, June 3, 1953.

It is sometimes true that methods that may be developed for use in normal states may need modifications when applied to pathological states. In general, however, this is not so, and medical technology, practically speaking, deals in the same scientific terms and uses the same tools and techniques in studying normal physiological processes or the variations of those processes under the influence of pathological conditions. For these reasons it has seemed proper to discuss a few problems and responsibilities in medical technology in relation to both physiology and pathology.

METHODOLOGY

In the research laboratories of both pathology and physiology, new and often extremely complex methods are constantly being developed, and it is on the basis of these new findings that medical progress depends to a considerable degree. Oftener than not, these methods and the results they produce never reach the routine practical level, but have their use as stepping stones in the elaboration of further research and ultimately to the final state that is the objective of all medical sciences. That is the treatment of the sick and the preservation of good health in the well.

Occasionally, out of the research laboratory comes a test or a method of measurement or some other technical procedure that can be used in the day-by-day study of patients, and here a grave responsibility rests. Before any such procedure is adopted as a routine method, it must be carefully scrutinized to be sure that it is as useful as possible before it is transferred to the clinical laboratory.

To fulfill its best functions as a practical routine method, a technique must be as simple as possible, it must employ as little and as simple apparatus as is consistent with required accuracy, and it must take as little time as possible in its performance. Now the critical judgment that is necessary to decide each of these points of requirement implies a broad knowledge of what is being measured by the method, and what the normal variations are, not only variations in what is being measured but also those variations that are inherent in the method itself. Such details are as much parts of a technique as the measurements of the reagents or the standardization of the apparatus. Yet it is surprising how seldom this information is included in the description of a technical procedure.

TOOLS OF MEDICAL TECHNOLOGY

The same general principles are equally applicable to the development of new apparatus employed in research. In the development of such mechanisms we are greatly benefited by our mutual association with research engineers and instrument designers and manufacturers, but it is the responsibility of our professions to see that, as far as we are able, every care is taken to be assured that apparatus that is to be used for clinical work is as well adapted to this sometimes modified use as is possible. Further, when such apparatus is translated from the research to the clinical laboratories, new sets of standards of control and variability must be set up.

These considerations unfortunately have been overlooked in many of the medical laboratory methods that have been used, often for many years. A reevaluation of some of these has already been made and others are under study, and it is very probable that the results of these studies will prompt a still more searching reevaluation of many of our common techniques. Such a study has been reported by Henry and associates,[1] in which the authors evaluate the effect of the errors introduced in several common chemical determinations by the simple procedure of pipetting. Such studies as this are as necessary as research into newer methods, and all new methods should be carefully submitted to such controls before being adopted for routine use.

A notable example of the failure of a medical laboratory technique to meet critical requirements is that found in one of the commonest, and often called "one of the simplest," techniques in the medical laboratory—the blood cell count. The method of counting blood cells has been changed in only minor ways since it was first described, and until quite recently the description of the method almost always contained the statement that the beginner should continue to make repeated counts on the same blood until successive counts could be made to agree within about 200,000 cells. In 1935 Berkson, Magath, and Hurn showed that such a standard of performance was impossible of accomplishment, and for the first time defined the normal variability of the total blood cell count as made with the hemocytometer.[2]

Another error that remained undetected for many years is the recently discovered error of 1 gm. of hemoglobin per milliliter of blood in the standardization of the British Haldane hemoglobinometer.[3] This explains for the first time why the "normal" English values for hemoglobin were always below those observed elsewhere.

Such an individual error, however, is only part of the far reaching and complex considerations that are inherent in even what is usually considered one of the simplest laboratory tests. A complete review of clinical hemoglobinometry by MacFate, MacFadyen, Stevenson, Copeland, and Sunderman will soon be published.[4] This review will reevaluate the whole subject. Such reviews as this are the best evidence of the intimate relationships that exist between the technical procedures used in the study of health and those used in disease. When these two examples among the very common laboratory methods are considered, it should add force and urgency to the necessity for control over all techniques, both old and new.

A number of years ago the American Society of Clinical Pathologists in cooperation with the United States Public Health Service undertook a national survey of the serologic testing for syphilis.[5] The findings of this survey were a shock to all concerned, but out of this study has

1. Henry, J. R.; Berkman, S.; Golub, O. J., and Segalove, M.: Analysis of Error in Clinical Chemical Determinations and Pipetting Procedures, Am. J. Clin. Path. **23**: 285-294 (March) 1953.

2. Berkson, J.; Magath, T. B., and Hurn, M.: Laboratory Standards in Relation to Chance Fluctuation of Erythrocyte Count as Estimated with the Hemocytometer, J. Am. Statist. A. **30**: 414-426 (June) 1935.

3. Lemberg, R., and Legge, J. W.: Hematin Compounds and Bile Pigments: Their Constitution, Metabolism, and Function, New York, Interscience Publishers, Inc., 1949, p. 296.

4. Sunderman, F. Wm., and others: Symposium on Clinical Hemoglobinometry, Am. J. Clin. Path. **23**: 519-598 (June) 1953.

5. Sanford, A. H.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States; Editorial, Am. J. Clin. Path. **5**: 339, 1935. Parran, T., and others: Efficiency of State and Local Laboratories in the Performance of Serodiagnostic Tests for Syphilis, Am. J. Clin. Path. **7**: 20-32 (Jan.) 1937.

come a new day in the use of serologic methods and a new concept of the establishment of controls over laboratory practice by such surveys. Similar surveys in other branches of laboratory techniques are now being used by state and national groups in an effort to further improve the standards of practice of medical technology.

In 1947 Belk and Sunderman made a survey in Pennsylvania at the request of the Committee on Laboratories of the Medical Society of the State of Pennsylvania, and reported surprisingly low standards in a number of common clinical chemical analyses.[6] Out of this study have come others, and many clinical laboratories now conduct continual controls over their routine work by means of services that provide standard solutions of several kinds. Recently Sunderman stated that, according to his continued observations, there is evidence that the standards of performance are showing a definite improvement over a wide area of the country.[7]

SEMANTICS OF MEDICAL TECHNOLOGY

Everyone who has attempted to write or read a description of a technical method is aware of the great difficulties encountered in clear expression of even very simple procedures. It is remarkable, in spite of this common and obvious hazard, that the written transmission of such information is as effective as it is. On the other hand, the literature is unfortunately filled with inadequate and often inaccurate descriptions of techniques that might otherwise be very useful and that may well be a danger in their published condition.

A few years ago a student of medical semantics selected a series of articles in which numerical values were used in attempts to prove certain medical scientific statements. When examined by suitable mathematical means, one-third of the papers were found to affirm the exact opposite of the facts that were supported by the measurements contained in the paper. Another third contained figures that were inconclusive, while only one-third had agreement between the numerical values and the conclusions of the authors.

A recent article on the "Role of Cybernetics in Physiology" by Cohn and Cohn [8] urges the importance of more effective communications in physiology and the profound importance of adequate controls that are inherent in such communications. The authors urge the necessity for the translation of the knowledge of one field into the terms and understandable modalities of related fields of knowledge. They further suggest that, as the breadth and complexities of sciences increase, there must be developed some more effective means than we now have of making the fundamentals of one field available and understandable to others. This is certainly pertinent to the present subject, for no matter how well conducted the techniques of research, and how carefully measured the values of the physiological state, they will have less than their needful effect if they are not translated into techniques and expressed in descriptive language and mathematically sound values that can be used in other fields of medicine.

PERSONNEL

In a series of articles dealing with the trends of technology in *Fortune*, a recent article predicts a technological revolution that may well dwarf any previous technical development in the application of the transistor, a device that promises to replace the vacuum tube and extend the uses of many of our most important mechanisms. However, it is unlikely that such mechanisms will ever replace the medical laboratory worker in physiology and pathology laboratories. Here the demand will be at least as great as it has been in the past for more and more well-qualified workers to carry out the myriad technical procedures that are the life blood of modern medicine.

It was the demand for such workers, and for some means to identify them, that prompted the American Society of Clinical Pathologists to establish the Board of Registry of Medical Technologists 25 years ago. Since then, 22,882 medical technologists have been certified. The great majority (18,018 in 1952) are still registered, and most of them are actively engaged in the practice of medical technology. According to a recent report [9] of the Council on Medical Education and Hospitals of the American Medical Association, 23,822 medical laboratory workers are currently employed by the hospitals of the United States. According to a recent study by the registry, in 1952 approximately 2,000 of the presently certified medical technologists were employed in medical schools and other research centers.

At the time of writing there were 538 approved schools of medical technology, with a yearly capacity of 4,116 students, which is an increase of 42 schools and 528 students over the previous year. This increase in both schools and their student capacity has continued uninterrupted since the first list of schools was published in the *American Journal of Clinical Pathology* in November, 1933.[10]

In spite of these encouraging trends, the supply of qualified medical laboratory workers has never met the demand, with the obvious dangers inherent in such a deficit in a field where incompetence may be so disastrous. The lack of properly trained workers is not by any means true in the field of medical technology alone, for approximately 20,000 kinds of employment are in vigorous and persistent competition to attract into their respective fields enough recruits to fill their increasing needs. These efforts at recruitment are being directed toward the smallest total number of 18 and 19-year-old men and women that has been in our population since 1890. It is small wonder, therefore, that medical technology, as well as all other areas of medical and ancillary medical education, is finding recruitment so difficult.

In a recent article, Associated Press Education Reporter David Marke told of the prospects for employment for June college graduates. These prospects continue to reflect the powerful forces that are being brought to bear on college students to enter various fields of employment and the continued and increasing demands for recruits. Reporter Marke states that Dean Fred Ajax, who is placement director of the Georgia School of Technology, estimates the demand in 1953 for graduates to be 75%

6. Belk, W. P., and Sunderman, F. Wm.: Survey of the Accuracy of Clinical Analyses in Clinical Laboratories, Am. J. Clin. Path. **17**: 853-861 (Nov.) 1947.

7. Sunderman, F. W.: Personal communication to the author.

8. Cohn, Stanton H., and Cohn, Sylva M.: The Role of Cybernetics in Physiology, Scient. Month. **76**: 85-89 (Feb.) 1953.

9. Arestad, F. H., and McGovern, M. A.: Hospital Service in the United States, J. A. M. A. **152**: 143-163 (May 9) 1953.

10. Board Report: Training Schools for Technicians Approved by the Board of Registry of the American Society of Clinical Pathologists, Am. J. Clin. Path. **3**: 484-488 (Nov.) 1933.

greater than in 1952. At Alabama Polytechnic Institute every senior received at least five job offers, and so it goes.

In almost all fields in which technologists of any kind are needed, greatly increased demands are found. Without exception placement officers report the demands for engineers and scientists as exceeding the supply by 5 to 1.

The salaries offered the newly graduated students also reflect the increased demand. Starting salaries are up, according to this report, from $25.00 to $50.00 over 1952. For graduates with bachelor degrees, starting salaries average about $375.00 a month, for persons with master's degrees $400.00, and for doctors of philosophy $500.00 and up. It is also notable and significant that nontechnical fields at the same educational levels offer on the average from $25.00 to $50.00 less in monthly salaries.

These facts are further accentuated by the efforts that large employers are making not only to attract newly graduated scientists but also to stimulate recruitment into their field of employment. Bethlehem Steel Corporation, as an example of this trend, has offered 45 colleges $3,000 for every graduate who completes its training course, and other companies offer such inducements as expense-paid tours of their plants and free transportation and moving expenses for new employees. Other industries are paying college placement offices a fee for every graduate recruited.

When we consider such matters as they affect all fields of employment of technical personnel, it is small wonder that medical technology is in such desperate straits. Salary levels in medical technology, in spite of continued increases, have always lagged behind others. No doubt this is largely because the majority of medical technologists are employed in hospitals, where salaries of all kinds, as a rule, are below comparable salaries elsewhere.

Fortunately, the postdepression rise in birth rate will soon begin to make available an increasing number of high school graduates. It is the mutual responsibility of all of us who are interested in the medical sciences to do all in our power to see that high school students are encouraged to enter the field of medical technology.

SCHOOLS OF MEDICAL TECHNOLOGY

It must be obvious that even the rapidly increasing number of approved schools of medical technology, with their present capacity of over 4,000 students a year, cannot meet the present needs, so it is urgently necessary for more schools to be established as soon as possible. Even though many schools have difficulty filling their classes, the more widely distributed the schools are the more students they will attract now. In the near future, when more students are available, the schools will have established their affiliations with colleges and universities, and will have had the opportunity to make their presence felt in the high schools of their vicinities.

If we believe, as I am sure we all must believe, that the future of medicine demands that medical technology be conducted by qualified laboratory workers, be it in the research laboratory, the clinical laboratory or elsewhere, then we must see that the rising generation is urged by every possible means to enter the profession of medical technology. We not only must see that the rising generation gets this message but must also see that the schools for their training are available for them, and that the courses and the teaching, and the textbooks, and the apparatus, and all the complex and ever-increasing armamentarium of all kinds of medical education are available for use by the young men and women when they present themselves.

The burden of carrying on the continuing recruitment campaign and in the organization and conduct of the schools must of necessity largely fall on the pathologist and the medical technologist who instruct the students. But everyone who knows the need must take an active part in individual recruitment and in making the field of the medical laboratory known and appreciated as widely as possible.

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CORTISONE INTERFERENCE WITH CALCIUM THERAPY IN HYPOPARATHYROIDISM

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At present there is not much information to be found in the literature concerning the effect of the adrenal steroid hormone cortisone on calcium metabolism. What has appeared seems somewhat contradictory. We therefore offer the following clinical observations, which tend to show that effective calcium therapy is not possible during cortisone administration. These observations seem to indicate that cortisone and calcium therapy counteract one another. Calcium excretion studies of the urine and feces were not made, but serum calcium and phosphorus studies were undertaken. Hypoparathyroidism is not common, and the striking interference with calcium therapy when cortisone was administered, with distressing symptoms of tetany suffered by the patient, prompts us to report this case.

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REPORT OF A CASE

A 51-year-old white woman was first seen on Nov. 9, 1948, with symptoms of hyperthyroidism due to an adenomatous goiter. This was removed by subtotal thyroidectomy on Dec. 8. The adenoma of the right lobe was retrotracheal and difficult to deliver. Three days later tetany of the fingers and toes accompanied by paresthesia of the extremities developed. The Chvostek and Trousseau signs were elicited. The serum calcium level was 7.62 mg. per 100 cc. (normal 9.0-11.5 mg.), and

the serum phosphorus level was 6.2 mg. (normal 3.0-4.5 mg.). Parathyroid extract, 300 units (3 cc.), was given intramuscularly daily for two days, and dihydrotachysterol (A. T. 10), two capsules (0.625 mg. each), was given daily. In addition, calcium was given both intravenously and orally. With this therapy the patient did well and was discharged on Dec. 15. The pathological report of the surgical specimen was thyroid adenoma. No parathyroid tissue was found.

On Dec. 27, the patient complained of tingling of her fingers and toes and was mentally sluggish. The serum calcium level at this time was 8.8 mg. and the basal metabolism rate was −1%. The dose of calcium orally was increased as was the dihydrotachysterol dosage. On Jan. 28, 1949, the patient was brought to the office in a state of mental confusion and complaining of severe cramps in her hands and feet. She was given calcium gluconate intravenously, with temporary relief, and was hospitalized. The serum calcium levels for the first few days of hospitalization were: Jan. 29, 7.15 mg. per 100 cc.; Jan. 30, 7.3 mg.; Feb. 3, 8.15 mg.; and Feb. 6, 8.72 mg. Therapy consisted of 300 units (3 cc.) parathyroid extract intramuscularly, calcium gluconate intravenously, and calcium lactate and dihydrotachysterol orally. The patient made an uneventful recovery. She went home and was given two dihydrotachysterol capsules and 3 gm. of calcium lactate daily. She checked her urine daily with the Sulkowitch reagent for calcium and had periodic serum calcium level determinations. A few of these were as follows:

Date	Serum Calcium Level in Mg. per 100 Cc.	Date	Serum Calcium Level in Mg. per 100 Cc.
Feb. 12, 1949	9.6	June 17, 1951	10.0
March 19	9.3	Dec. 6	8.8
April 1	10.1	Dec. 27	9.0
July 17, 1950	10.9	March 7, 1952	8.9
Nov. 16	8.3	Nov. 1	8.3
Nov. 29	9.2	Nov. 7	8.2

During the period from February, 1949, through October, 1952, the patient continued her therapy, at times taking less dihydrotachysterol, depending on the results of the urine calcium (Sulkowitch) study.

On Oct. 24, 1952, cortisone therapy was started, 25 mg. twice a day, for multiple osteoarthritis. The patient's appetite improved, as did the arthritis; however, on Oct. 31 the patient again complained of paresthesia and cramps in her hands and feet. Her appetite and semi-euphoric state persisted. The serum calcium level at this time was 8.3 mg. The dihydrotachysterol dosage was increased and calcium gluconate was given intravenously. However, the signs and symptoms of tetany became worse and Chvostek and Trousseau signs could be elicited. The antitetany therapy was intensified, and the patient now received parathyroid extract intramuscularly (300 units); dihydrotachysterol, 3 capsules daily; calcium gluconate intravenously; and 6 gm. of Neocalglucon (a calcium gluconate solution) daily. The patient became increasingly confused and found it difficult to answer questions. The tetanic spasms in her hands and feet became severer. On Nov. 8, she was again hospitalized. The serum calcium level at this time was 8.3 mg., the inorganic serum phosphorus level 6.1 mg., the alkaline phosphatase level 3.2 mg. (normal up to 13 units), and serum potassium level 15.6 mg. (normal 14-20 mg.). The electrocardiographic Q-T interval was 0.46 second in duration.

During this time the patient continued to receive the large doses of calcium orally and intravenously, dihydrotachysterol, parathyroid extract, and cortisone, 25 mg. twice a day. The Chvostek and Trousseau signs persisted, as did the mental dulness and depression. The patient's skin was dry, so much so that a superficial ulcer developed on the outer right thigh such as is seen in chronic trophic changes in hypoparathyroidism.

In reviewing the therapy, one of us (R. C. M.) was reminded of a physician with myasthenia gravis whom he had treated with six implanted pellets of desoxycorticosterone acetate (150 mg. each). One of the pellets was purposely crushed, and within two weeks marked polydipsia and polyuria developed. Coincident with these symptoms, symptoms of tetany developed, with Trousseau and Chvostek signs. The serum calcium level was 8 mg. and the phosphorus level was 3.9 mg. The patient showed pronounced muscular weakness. These signs and symptoms of tetany continued to be manifested for two months. It was felt that the desoxycorticosterone acetate was in some way interfering with the calcium and phosphorus metabolism, thus producing the tetany.

The thought that perhaps cortisone was producing the difficulty in controlling our patient with hypoparathyroidism led to stopping cortisone therapy. Within three days the patient was markedly improved. The signs and symptoms of tetany disappeared. The serum calcium level on the third day after cortisone therapy was stopped was 10.1 mg. and five days later 10.5 mg. At present the patient is being well maintained on 2 (0.625 mg.) capsules of dihydrotachysterol daily and 12 gm. of calcium gluconate daily. Seven serum calcium level determinations between the interruption in cortisone therapy and June 7, 1953, gave an average reading of 9.7 mg.

This case, in our opinion, demonstrates that the adrenal cortical steroids either decrease the absorption or increase the excretion of calcium or both. Despite the administration of calcium parenterally and orally, dihydrotachysterol, and parathyroid extract, the hypocalcemic state persisted. Soffer,[1] from observations made on patients with Cushing's syndrome and from observations by others [2] on patients treated with corticotropin, concluded that cortisone and corticotropin produced an increased excretion and a reduced absorption of calcium in the intestinal tract. The same was true of phosphorus but to a lesser extent.

We had occasion to observe a case of primary nontropical sprue in a 23-year-old white woman who came to us after being treated elsewhere with cortisone. She gave a history of diarrhea, weight loss, weakness, anemia, tetanic spasms of the fingers, and swelling of the lower extremities. The patient had not made any progress with various forms of therapy and therefore cortisone therapy was started. While cortisone was being given (100 mg. daily orally), the edema became generalized with swelling of hands and face and the tetanic spasms became much more severe, involving both upper and lower extremities. The use of calcium orally and intravenously along with a hydrochloric acid preparation (Acidulin) and vitamin D relieved the tetanic symptoms to some extent. Subsequently when cortisone therapy was stopped the tetanic spasms were well controlled by the calcium, hydrochloric acid preparation and vitamin D preparations. When the patient came under our care some weeks after the cessation of cortisone therapy, she had generalized anasarca. The total protein was 4.23 mg. per 100 cc., albumin 2.86 mg., globulin 1.37 mg. and albumin-globulin ratio 2:1.

Subsequently signs and symptoms of tetany developed, and the patient was hospitalized. She was given several blood transfusions to elevate the serum protein levels and to correct the anemia. Since that time she has been well

1. Soffer, L. J.: ACTH and Cortisone: Physiologic and Clinical Considerations, M. Clin. North America **36**: 791-809 (May) 1952.

2. Kinsell, L. W., and others: Metabolic Effects of Peptide Mixture Derived from ACTH (Li) in Comparison with Those Resulting from Whole ACTH Administration in a Human Subject, in Proceedings of First ACTH Clinical Conference, Philadelphia, Blakiston & Co., 1950, p. 70.

controlled with the usual liver extract administered parenterally, folic acid, calcium administered orally, vitamin D with liberal doses of dilute hydrochloric acid, multiple vitamins, and a high protein, moderate carbohydrate, and low fat diet. She is at the present time seven months pregnant and is feeling well.

It would seem that in this case the cortisone interfered with the calcium metabolism and intensified an already hypocalcemic state. That a low serum protein level may have been instrumental in producing the hypocalcemia must be admitted. As is known, hypoproteinemia causes a decrease in the total serum calcium because of a correspondingly low protein-bound calcium level. Cortisone is thought to produce a negative nitrogen balance through interference with protein synthesis from amino acids [3] and by increasing protein catabolism,[1] indirectly producing tetany. One would doubt that the factor of alkalosis played a part in the symptoms of tetany because there was no history of vomiting, the frequency of stools was four to six per day, and, in addition, the patient was receiving hydrochloric acid therapy.

Colcher and co-workers [4] in their series of eight cases of sprue treated with cortisone and corticotropin noted signs of tetany in three of the patients who were receiving cortisone. This they felt was due to hypochloremic alkalosis and associated hypocalcemia. The tetany in their cases was controlled by use of ammonium chloride and oral calcium. One of us (A. L. S.) treated a patient with ulcerative colitis with cortisone and later with corticotropin. Clinical tetany also developed during the period of cortisone administration. The symptoms were readily controlled by calcium administered orally and intravenously. Here too, after the cortisone therapy was discontinued, clinical tetany was no longer present.

COMMENT

From the clinical observations we have made, it would seem reasonable to conclude that cortisone affects calcium metabolism so that a negative calcium balance is produced. When there is already present a tendency toward tetany, cortisone therapy will increase the tetanic hazard. This mechanism is probably due to a combination of cortisone effects in (*a*) decreasing calcium absorption, (*b*) increasing calcium excretion, and (*c*) lowering the total serum calcium secondary to decreased serum protein resulting in a lowering of the protein-bound calcium. We may assume that the combination of these effects on calcium metabolism is not great enough in the average patient receiving cortisone therapy to produce clinical evidence of tetany unless there is already present an underlying condition that tends to produce tetany in its own right, such as seen in hypoparathyroidism, ulcerative colitis with poor calcium absorption, or a low serum protein level with a low serum-bound calcium level.

SUMMARY AND CONCLUSIONS

It was observed that the simultaneous administration of cortisone and drugs to overcome hypocalcemia resulted in nullifying the latter form of therapy. A case is reported of a 51-year-old woman who had postoperative hypoparathyroidism and was well maintained with drugs to overcome the hypocalcemia. The administration of cortisone for rheumatoid arthritis produced a rapid drop in serum calcium level, an elevation of serum phosphorus level, and the signs and symptoms of tetany with mental confusion. Discontinuance of cortisone therapy resulted in a prompt rise of the serum calcium, a drop in the serum phosphorus, disappearance of the signs and symptoms of tetany, and return to a normal mental state.

The antagonism between an adrenal steroid hormone —desoxycorticosterone acetate—and calcium-phosphorus metabolism was also observed in a physician in whom desoxycorticosterone acetate pellets had been crushed during implantation. Two other patients, one with nontropical sprue and one with ulcerative colitis, showed interference with calcium metabolism during the administration of cortisone therapy. It would seem from these clinical observations that cortisone interferes with calcium metabolism.

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3. Irons, E. N.: Recent Studies on ACTH and Cortisone, M. Clin. North America **36**: 229-246 (Jan.) 1952.

4. Colcher, H.; Drachman, S. R., and Adlersberg, D.: Management of Intractable Sprue with Cortisone and Adrenocorticotropin (ACTH), Ann. Int. Med. **38**: 554-568 (March) 1953.

COMMUNITY HEALTH PLANNING

STUDY OF "ATOMIC CITY" (RICHLAND, WASH.)

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Death rates in the "Atomic City" of Richland, Wash., based on a five year study, are one-half those of the nation, after correcting for population age differences. This represents a great decrease in suffering and a tremendous economic saving to this city of 24,000 persons. Nine factors are considered likely to have contributed most to the attainment of these results. A uniquely planned and integrated medical program, which has been operating during the nine years of this city's life, is felt to be one of the factors that has contributed to this record, of which the citizens are justly proud. This article is written to describe the medical program, because other American communities may profit from Richland's experience. Five years is a relatively short period for a statistical comparison of this type; however, we feel that this early study will be valuable to compare this period with the next period when the community will probably be incorporated.

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In the search for more satisfactory health for their people, many nations of the world have turned to socialized medicine. Strenuous efforts to socialize medicine are being made in this country, even though the United States enjoys the finest health of any large nation in the world. The answer to much of the socialized medicine problem lies in sound community health planning, participated in by all elements of the community. National health is simply the sum total of the health in all local areas. American initiative and ability applied at the local level should prove far more effective in providing good health and good medical care than a regimented national program, supported by higher and higher taxes. This article describes such an integrated program of (*a*) public health, (*b*) a community hospital center, (*c*) industrial medicine, and (*d*) private medical practice featuring very adequate specialty coverage.

In 1944, a modern city was built in the semiarid waste lands of southeastern Washington to house the workers of the secret Hanford Works, which was to produce plutonium for atom bombs. The town and plant were built and operated by the du Pont Company for the U. S. Army. In 1946, the program was turned over to the General Electric Company to operate for the U. S. Atomic Energy Commission. At present, the municipal functions of this city are managed by the company. The industry and the town have continued to grow, since it is predicted that atomic energy's peaceful uses in medicine and industry may outstrip its war uses. The population of Richland is now 24,000, and it is growing rapidly. The residents are planning for eventual private ownership of property and incorporation of the community.

Complete, integrated medical services have been made available by the industry that has operated the plant and the community for the government for a period of nine years. These services consisted of public health, industrial medicine, hospital, and, for the first six years, general patient care. With all facilities closely grouped and with activities coordinated, the community medical center idea has been a reality.

In the early years of the project, there was no assurance that the venture might not be short-lived. Under such conditions, general medical care was supplied by medical specialists and general physicians, operating under guaranteed income. As soon as it became apparent that the community would become stable, private practice by physicians replaced the old system. This occurred in 1950. The incentive of private practice has resulted in a decrease in the number of physicians required by about 35%, without any apparent change in the quality of care and with greater patient satisfaction. Salaries of the employed physicians were based on a 40-hour work week. Emergency night and Sunday calls were taken by the physicians on call. A recent survey by *Medical Economics* magazine indicated that the American physician in private practice works an average of 58 hours per week.[1] The survey also indicated the value of supporting personnel, in that the physician who employs one or more aids spends 40% less time per patient than does the doctor without assistants. From our experience, we predict that, even with an efficient supporting system, any medical program with salaried physicians will require one-third more physicians.

MEDICAL DEPARTMENT

The present organization of the medical department has changed little in essential features since its inception. The director is a physician who reports to the project manager. His administrative staff is composed of a physician who is head of public health, a physician who is director of industrial medicine, and an administrator for the hospital. Total employees of the medical department number 273, or 0.8 employee per 100 population served. Community physicians and dentists are members of the hospital staff and rent office space in adjoining clinic buildings. Close liaison is maintained with voluntary health agencies, such as the Bicounty Anti-tuberculosis league; county chapter of the National Foundation for Infantile Paralysis; Women's Field Army American Cancer Society; county chapter of the American Red Cross; local Community Chest; county chapter of the National Heart Society; county chapter of the National Society for Crippled Children and Adults; Community Health Council; and service clubs.

PUBLIC HEALTH

In general, Dr. C. E. A. Winslow's scope of public health has been accepted as the basis of the program in Richland.[2] This includes "the art and science of preventing disease, prolonging life and promoting physical and mental health through organized community effort." The six basic functions—vital statistics, communicable disease control, environmental sanitation, public health laboratory services, maternal, infant, and child hygiene, and health education—have been established. In addition, bedside nursing, school nursing, mosquito control, and welfare services have been incorporated. The welfare function deals primarily in the areas of family service, child welfare, and medical social work. Direct monetary relief is furnished by funds granted through the local community chest or county agencies. The basic public health program costs about $2.50 per person or $9.25 per family per year. This amounts to three cents a day, per family, the cost of a postage stamp. This is the amount that most public authorities agree is necessary for a good public health program.[3] Additional costs for a bedside nursing program, school nursing, mosquito control, etc., will depend upon local conditions. There are 20 employees in the public health and welfare program.

INDUSTRIAL MEDICINE

Industrial medical practice has been organized with the prime objective of preventing job-connected and personal illness and accidents and promoting physical and mental health of employees. The preventive objective has been given added impetus by the potential radiation hazard in the atomic project and the knowledge that treatment of the damaging effects of radiation is very ineffective. This absence of effective therapy, of course, also exists in many far-advanced nonoccupational disease states and can be alleviated by practicing the principles of preventive medicine. The concept that medicine

1. The Average U. S. Physician, M. Economics **30**: 78 (Oct.) 1952; Your Economic Weather Vane, ibid. **30**: 91 (Feb.) 1953.
2. Winslow, C. E. A.: Untilled Field of Public Health, Mod. Med. **2**: 183 (March) 1920.
3. Hiscock, I. V.: Community Health Organization, ed. 4, Cambridge, Mass., Commonwealth Fund, 1950.

has far too long concerned itself with treatment at the expense of prevention, which is really easier in many cases, is literally accepted. This concept has been observed to produce benefits for both employee and company.

More specifically, this plan is carried out through (1) medical acitvities that concern the individual employee and (2) combined medical and engineering activities that concern the working environment. Activities that are entirely medical include preplacement and periodic medical examinations, provision for first aid, medical and surgical service while on the job, and health education, which includes mental health and health conservation. The combined medical and engineering functions include control of environmental conditions in work situations insofar as they may affect the health of employees, such as ventilation, atmospheric pollutions, radiant energy involved in atomic fission, or exposure to toxic chemicals or materials. The industrial medical program is designed to materially reduce (1) occupational disease, (2) accident frequency, (3) personal illness, (4) absenteeism, (5) compensation costs, and (6) labor turnover and to improve employee personal relations.

HOSPITAL

Kadlec, a 106-bed hospital, is registered with the Council on Hospitals and Education of the American Medical Association and is approved by the American College of Surgeons. It is also approved for residency in general practice and internship. The hospital is a member of the Washington State Hospital Association and the American Hospital Association and derives great benefit from these associations, which have played such an important role in the tremendous growth and progress of American hospitals. Nursing hours per patient day are maintained at about 3.5 for the general nursing services and 4 for obstetrics. The number of hospital employees per hospital patient is kept slightly less than two. The occupancy factor is maintained at 70 to 80% except during population peaks due to temporary large construction activity, when the occupancy factor sometimes exceeds 100%. The ratio of beds to population eligible for hospital care is 3 beds per 1,000 persons.

The hospital is the center of medical activities. Its well-equipped x-ray center, directed by a radiologist, serves the hospital patients, the physicians' private outpatients, public health, and employees. Four by five inch (10.2 by 12.7 cm.) photoroentgen chest films are routine for hospital admissions, new employees, and annual examinations of employees. An exception to this rule applies to employees whose work is in areas of potential exposure to radiation. They receive 14 by 17 in. (66 by 73.7 cm.) chest films because of the lower exposure. A visit every two years by the area mobile x-ray unit, under the direction of the Bicounty Anti-Tuberculosis League, adds to the over-all coverage for chest roentgenograms. In similar manner, the clinical laboratory under the direction of the pathologist furnishes services to all segments of the medical program. In an isolated community of this size, it would not be economically feasible to have a pathologist or a radiologist unless they handled most of this work. The pathologist also acts as consultant in experimental work aimed at better evaluation of the plant radiation hazards.

The medical library has about 1,100 volumes, subscribes to more than 100 medical journals, and has access to the medical school libraries of the universities of Washington and Oregon. Physicians, therefore, have excellent library facilities, although they are in an isolated location. The reading room of the library, with a seating capacity of 50 persons, serves as a meeting place for the medical staff and for groups interested in community health.

VITAL STATISTICS

During the past five years the actual death rate per 1,000 population in Richland has been only one-fourth that of the nation. For the period 1948-1952, the actual death rates per 1,000 population were 2.1, 2.3, 1.5, 2, and 3 for the five respective years. The average for this five years period was 2.2. For the United States as a whole, the death rate for the white population in 1950 [4] was 9.5. This comparison does not take into account the unusual age distribution of the population of Richland as compared to the national distribution. To adjust for this effect, it was necessary to determine what the Richland death rate would have been for each year and for the five years if the national rate for each age group had prevailed in Richland (table 1).

TABLE 1.—*Richland Five Year Expected Death Rate and Actual Death Rate*

	1948	1949	1950	1951	1952	5 Year Average
Richland expected death rate per 1,000 population	4.4	4.2	4.4	4.4	4.6	4.4
Richland actual death rate per 1,000 population	2.1	2.3	1.5	2.0	3.0	2.2

TABLE 2.—*Richland Five Year Specific Age Death Rate and National Rate, 1950*

Age Group	Richland Five Year Rate per 1,000 Population	National Rate, 1950, per 1,000 Population (White)
Under 1	16.8	28.9
1-14	0.4	0.8
15-24	0.7	1.1
25-34	0.4	1.5
35-44	1.2	3.2
45-54	5.2	7.6
55-64	9.8	17.6
65+	34.9	66.2

Mr. L. G. Waters of our statistics unit, who made these statistical comparisons, concludes: "Comparing these expected rates with Richland's actual rates, there is conclusive statistical evidence that the Richland rates were lower in every case." It will be noted that the actual death rate per thousand for the five year period was 2.2, which is one-half the expected rate of 4.4 based on the national experience. Five year death rates by age groups in Richland are lower by statistically significant factors in each group (table 2).

Since the State of Washington death rates have followed the national rates rather closely, the comparison of Richland rates with State of Washington rates would probably differ little from the comparison with national

4. Statistical Abstract of the United States, 1951, ed. 72, U. S. Bureau of the Census, 1951, p. 262.

rates. It is of interest to note that during the nine year period since the inception of the medical program, more than 6,000 Richland babies have been delivered at Kadlec Hospital without a maternal fatality.

CONTRIBUTING FACTORS

The health of a community is the result of many factors. What differences in Richland have contributed to the above results? The high economic status of the people and the well-integrated program of preventive and treatment medicine are felt to be factors of major importance. Following are nine factors that are discussed from the standpoint of their contribution to the results given above.

Economic Status.—Essentially there is no medical indigency in Richland. Eligibility for housing is contingent on employment in project-connected work; hence, every family has at least one breadwinner. This has less importance than it had in the past, since good medical care, food, and shelter are assured to even the poorest families today. Overweight in the prosperous is perhaps more serious than nutritional lack in the indigent.

Good Medical Specialty Coverage and Adequate Number of Physicians.—The fact that there has been no maternal death here, with more than 6,000 deliveries, the low infant mortality rate (five year average of 16.5), and the low hospital death rate (0.35%) are all evidence that a sufficient number of specialists favorably influence the over-all health results. Dr. Howard A. Rusk's studies indicate that in the United States a physician serves an average of 850 persons.[5] Richland's results have been obtained with one physician for each 1,200 persons, counting every physician. If we deduct physicians doing administrative, public health, and industrial medicine, it leaves one physician in clinical practice for each 1,800 persons. This confirms the contention that the desirable ratio of physicians to population has a wide range, depending upon local conditions. About one-third more physicians and dentists were required when they were working on a salary basis.

Industrial Medicine.—More than 90% of the employed persons, including the 9,000 General Electric employees in the community, receive good industrial medical care, as indicated by approval of this phase of our program by the Industrial Medical Association. Disease is detected in an earlier corrective stage, through preplacement and periodic examinations, and employees are referred to the family physician or dentist for correction. Assistance and advice is given to employees by industrial physicians and nurses in matters of personal hygiene, emotional disturbance, and personal illness. The quick treatment of even the most minor injury decreases the chance for infection and develops an attentiveness to such matters, which influences care of such injuries that occur at home. Formal and informal health education spread the knowledge necessary for the intelligent use of the many health facilities that are easily available. In these and a host of other ways, the employee is assisted in maintaining good mental and physical health. Results are improved human relations, decreased labor turnover and absenteeism, and greater efficiency of employees.

Industrial hygienists, radiological science workers, safety engineers, and health-conscious supervisors and workers contribute to making the plant a safe and healthful working place. The health and safety practices of the worker undoubtedly have a great influence on the attitudes and practices of the whole family. Since Richland is a "one industry community," the health practices of this industry have a tremendous influence on the health of the community. Absenteeism due to sickness among project employees has averaged 1.58% during the last six years, which is about half that experienced by industry generally. The national estimate is that 8 days are lost per year by men and 12 by women,[6] whereas, at Hanford Works, 3.9 days are lost per year by men and 7.43 by women.

Since General Electric employees in this project, with one or more years of service, are paid for excused absence due to sickness, the actual savings due to the lower sickness absentee rate are sufficient to pay the entire cost of the industrial medical program, which amounts to about $45 per employee annually.

Many large industries have found that a good industrial medical program more than pays for itself in reduced absenteeism and employee turnover, decreased spoilage, and improved human relations. If all industries, large and small, would install improved industrial medical programs, the influence on employee health and on general community health would be tremendous, and industrial leaders would be aiding in preventing the first major phase in the socialization of our country.

Medical Insurance.—Over 99% of the 9,000 employees of General Electric at Hanford Works and more than 90% of their dependents are covered by prepaid hospital and medical-surgical insurance. The premiums are paid partly by the employee and partly by the company. Other employed persons have Blue Cross or prepayment insurance, so that well over 90% of the citizens of Richland may enter the hospital, knowing that their hospital and surgical bills will be almost entirely paid. Fear of a large hospital bill often deters a person from entering the hospital until so late in the disease that his recovery is greatly delayed or even prevented. Because this fear is greatly allayed, Richland residents had an annual hospital admission rate in 1950 of 185 per thousand population. The state had a rate 37% lower than this; however, the state's average hospital stay was 38% higher than Richland's average stay of 5.3 days.[7] While more persons enter the hospital, the shorter average stay of each results in the same total usage of the hospital and the same bed requirement as other hospitals in the state. Early effective treatment results in fewer deaths, shorter convalescence, and decreased absenteeism.

Population Age and Racial Differences.—Since, in this study, comparisons of the Richland results with those of the state or nation are made by comparing persons in the same specific age groups, age is not a factor. Stated differently, since we have more young persons

5. Rusk, H. A.: Procurement, Assignment, and Utilization of Reserve Medical Officers, J. A. M. A. **147**: 723 (Oct. 20) 1951.

6. Maxcy, K. F.: Rosenau Preventive Medicine and Hygiene, ed. 7, New York, Appleton-Century-Crofts, Inc., 1951, p. 1098.

7. Powers, L. E.; Bennett, B. M., and Turner, E. L.: Acute Hospital Bed Needs, Northwest Med. **51**: 23 (Jan.) 1952.

and fewer old persons, our mortality rate is expected to be 4.4 per 1,000 instead of 9.5 per 1,000 as for the nation. Difference in death rate due to racial differences has been minimized by comparing the Richland rate with the national rate for white persons, since this includes more than 99% of the residents of Richland.

Selection of Personnel for Hanford Project.—Persons were recruited for this project from all walks of life and from every state in the union. Because of a tight labor market, many persons were employed who would ordinarily have been considered unfit from a physical standpoint. Many physically handicapped persons were placed on jobs commensurate with their physical limitations, but the rejection rate for new employees was approximately 2%. Special selection of persons for the project would, therefore, appear to have little effect on the mortality rates.

Public Health Program.—The program in Richland is comprehensive but does not include any practices that are not recommended by recognized leaders in the field of public health. That results are surprisingly good, as compared to the average American community, is merely an indication that the average American community lacks some essential public health services. Since the financial requirements for a good public health program are pitifully small in comparison with the gains in longer, happier lives, it becomes obvious that the average American community requires something to awaken it to its needs. Perhaps physicians need to use evangelism to save bodies as ministers use it to save souls. As in other matters, it is so easy to endeavor to shift the responsibility to the state or federal level, failing to realize that to achieve the same end we merely add to the bureaucratic duplication and red tape and needlessly multiply the tax burden.

Persons should be educated to take care of their medical needs at the local level. Richland's public health funds are presently supplied directly by the federal government. Richland is expected to become a locally administered municipality in the near future. It will be interesting to see if the people will tax themselves, at the local level, sufficiently to continue the program as it is presently conducted. We are confident that this challenge will be met. The average American family spends 30 cents per day for tobacco and 60 cents per day for alcoholic beverages.[8] It is not asking too much of the average American family to spend 3 cents per day for a reasonably adequate public health program.

Integration of Medical Services.—At Richland, industrial medical services, including examinations and dispensary services, are administered in one section of the hospital. The public health building and the clinics for private medical specialists and dentists are on the "campus" in close proximity to the hospital. X-ray facilities under the direction of a board radiologist and laboratory services headed by a board pathologist are available for industrial medicine, public health, hospital patients, and outpatients. The industrial medical dispensary serves as the emergency admitting center for the hospital. The public health chief, in addition to the usual duties, assists in planning hospital expansion and health education for employees as well as the general public.

If John Smith's preemployment chest film indicates that he has early active tuberculosis, he is handled jointly by the industrial physician, the public health physician, and the private physician. Because of the proximity of buildings, all of these persons may quickly review the roentgenograms, check the medical records, make necessary physical and laboratory examinations, and arrange for proper institutional care. The public health officer and the industrial physician check family and close contacts at work for possible tuberculosis. These are all simple procedures, recognized as good practice in all communities but made complex by division of responsibility, failure in communication, and lack of understanding of the part each group plays in handling the patient. Had Mr. Smith been one of the many workers not covered by a reasonably good program of industrial medicine, his tuberculosis might have reached an incurable stage before detection and many persons might have been infected before the source of infection was discovered. Or the industrial physician might have told the prospective employee to seek care of his private physician, and, without follow-up, this might not have been done. If it had been done, the public health officer, located at the other end of the city, might not have been notified and case study for detection of sources would have been omitted. Or the community, being one of the 25% of communities who fail to appropriate funds for a basic minimum program,[9] might not have a public health officer.

ECONOMIC VALUE

The achievement in Richland is merely one example of how an integrated service, applying the same management methods to health programs that are applied in operating a multibillion dollar business, accomplishes things that sometimes are missed in the average American community. It is believed that many of the health measures listed above have assisted in preventing the deaths of an average of 2.2 persons in each thousand population, or 46 persons in Richland, a community of 24,000. These persons whose lives are lengthened can produce and contribute to family and community economy for a greatly extended period. What is this worth to the community?

Most persons appreciate the reduction in human suffering that has resulted from a good program of constructive medicine. Many have tried to evaluate man—to put a price on his economic worth. Hanlon,[10] drawing upon the work of Dublin and Lotka,[11] has arrived at the approximate money values for man at various ages. This value is an approximation of the average net earning power in terms of money of a person for the rest of his expected life span. Somewhat similar figures are used in compensating a family for the accidental death of an employee at work. We have done some interpolating for ages above 45, since Hanlon's table includes only ages up to

8. Dickinson, F. G.: Medical Care Expenditures, Prices and Quantity, 1930-1952, J. A. M. A. **147**: 1354 (Dec. 1) 1951.

9. Halverson, W. T.: Administrative Practice, Reports of Committees, Am. J. Pub. Health **42**: 49 (May, pt. 2) 1952.

10. Hanlon, J. J.: Principles of Public Health Administration, St. Louis, C. V. Mosby Company, 1950.

11. Dublin, L. I., and Lotka, A. J.: Money Value of a Man, ed. 2, New York, Ronald Press Co., 1946.

45 years. For the age groups under 1 year, 1-14, 15-24, 25-34, 35-44, 45-54, 55-64, and 65 and over, the mid-values of lives are $800, $8,000, $18,000, $20,000, $15,000, $10,000, $6,000, and $3,000 for the respective age groups.

Taking the reduced number of deaths in Richland in each age group and multiplying by the appropriate money value for a person in this group, one arrives at a money value for the lives extended per thousand population; for example, in the age group 25-34 there are about 5,000 persons in Richland, and the average number of deaths annually has been two. If the death rate in this age group had been the same as for the nation as a whole, there would have been eight deaths in Richland. Subtracting these two, we find that the various combination of efforts has resulted in six fewer deaths annually in this age group. Multiplying by the estimated value of extending a life in this age group ($20,000), we arrive at a dollar saving of $120,000. Repeating this type of arithmetic for all age groups, we find that there is presently an average annual saving of $420,000. The figures were based on 1940 values. The value of a dollar is now approximately one-half what it was in 1940 in terms of living costs. It would seem appropriate to multiply these values by two, giving an annual saving greater than three-quarters of a million dollars.

Richland has no medical resources that are not available to the average community. The problem has been simpler than in most communities. The small investment needed for a good health program is within the reach of any American community. The average American is being made increasingly aware by such studies as those mentioned above that minor savings at the expense of the public health program is, as Hanlon expresses it, "penny wisdom and pound foolishness." To an increasing extent, industries are realizing that a good industrial medical program more than pays for itself in decreased absenteeism, increased employee efficiency, and decreased turnover. Improved community health, as indicated in this study, is an added dividend.

Prepaid medical care with the wholehearted support or medicine, hospitals, and organized groups throughout the country, is expanding at a tremendous rate. Voluntary health insurance for more than 90% of the people in Richland has definitely assisted in reducing mortality rates. It is hoped that this will serve as a stimulus for all communities to attain such coverage. The good progress that is being made is indicated by the recent report of the Council on Medical Service of the American Medical Association that there was ample reason to predict that 90 million persons would be covered by some form of prepaid voluntary health protection by the end of 1952.[12]

Every community seeks to attain as smooth an integration of its health service as possible. We are sure that the coordination and integration of medical services here have contributed much to the health of our residents. The high degree of specialty coverage that we have here is not attainable in all communities; however, many communities would benefit by a greater degree of specialty coverage than they now have, and efforts of civic groups along this line are usually fruitful.

SUMMARY

Conditions in Richland have been such that we are fortunate enough to have a well-integrated program of public health, adequate hospital facilities, specialty as well as general practice coverage, a good industrial medical program for most employed persons, and voluntary health insurance for more than 90% of the residents. Over a five year period, such a program, along with a high economic status of the people, has contributed to reduce mortality rates to half those of the nation, and this has resulted in estimated saving of nearly three-quarters of a million dollars annually. Follow-up studies will be made to see whether this trend persists.

Kadlec Hospital (Dr. Norwood).

12. Report of Meeting of Council on Medical Service, J. A. M. A. **150**: 698 (Oct. 18) 1952.

CLINICAL NOTES

PHYSICAL SIGN OF TIGHT MITRAL STENOSIS

AID IN SELECTION OF PATIENTS FOR VALVULOTOMY

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Surgical repair of mitral stenosis has been proved beneficial in suitable subjects. Many patients who have mitral stenosis of moderate degree may engage in normal activities and live a normal life; they do not require surgical treatment. Only those with tight mitral stenosis should be subjected to surgery.[1]

Ravin and associates [1b] studied 17 patients in whom the diagnosis of tight mitral stenosis was confirmed by surgical exploration. These authors listed right ventricular hypertrophy as one of the significant features of tight mitral stenosis. They pointed out the difficulty that is occasionally encountered in assessing right ventricular hypertrophy by roentgenologic study; they further stressed that electrocardiographic evidence of right ventricular hypertrophy was present only in a minority of their patients.

A physical sign of right ventricular hypertrophy can often be demonstrated. It is characterized by a heaving pulsation of the precordial area felt during systole pri-

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1. (*a*) Friedberg, C. K.: Diseases of the Heart, Philadelphia, W. B. Saunders Company, 1949, p. 584. Andrus, E. C.: Selection of Patients with Mitral Stenosis for Surgical Treatment (Valvulotomy), Mod. Concepts Cardiovas. Dis. **20**: 116 (Dec.) 1951. Bland, E. F.: Surgery for Mitral Stenosis, Circulation **5**: 290 (Feb.) 1952. Harken, D. E., and others: The Responsibility of the Physician in the Selection of Patients with Mitral Stenosis for Surgical Treatment, ibid. **5**: 349 (March) 1952. (*b*) Ravin, A., and others: Diagnosis of Tight Mitral Stenosis, J. A. M. A. **149**: 1079 (July 19) 1952. (*c*) Griffith, G. C., and others: The Selection and Medical Management of Patients with Mitral Stenosis Treated by Commissurotomy, Circulation **7**: 30 (Jan.) 1953.

marily in the left parasternal region.[2] Viar and Harrison [3] found the precordial pulsation more reliable for the diagnosis of right ventricular hypertrophy than electrocardiographic and roentgenologic evidence. The pulsation is usually absent if hypertrophy of the right ventricle is slight, or, if hypertrophy is marked, it is of the concentric type, as, for instance, in patients with compensated pulmonary stenosis. It is most frequently encountered in mitral valve lesions in which dilatation of the left atrium

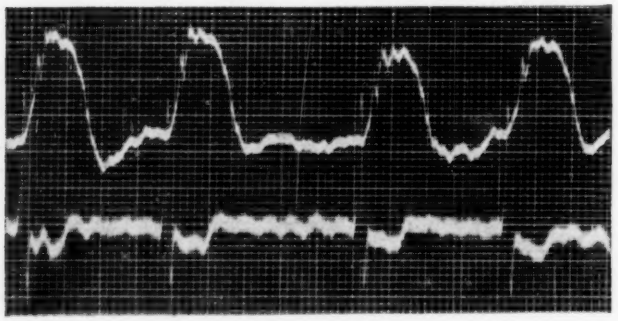

Fig. 1.—Upper tracing represents a displacement curve of the precordium; curve rises steeply at the onset of systole and forms a plateau similar to the palpable systolic elevation. Upward movement of the curve indicates lifting of the chest wall. Electrocardiogram below.

forces the heart toward the anterior chest wall, thus enabling the enlarged right ventricle to transmit its forceful pulsation to the precordial region. When clinical signs point to mitral stenosis, heaving pulsation in the precordial area invariably indicates marked narrowing of the mitral orifice.[2] The validity of this view has been tested in recent years by observations made during valvulotomy. The precordial pulsation was present in 15 of 17 patients in whom the diagnosis of tight mitral stenosis was later confirmed by surgery. In the two patients in whom the precordial pulsation was absent, tight mitral stenosis was associated with tricuspid regurgitation. The latter is known to cause a depression of the precordium during systole.[4]

Heaving precordial pulsation in patients with mitral stenosis has proved to be a valuable aid in the selection of cases for surgery. This simple clinical sign is illustrated by the following case reports.

REPORT OF CASES

CASE 1.—A 37-year-old housewife was admitted to the hospital on Oct. 2, 1952. The patient gave no history of rheumatic fever. At the age of 22, she began to tire easily while doing house work. At 25, she first learned that she had a heart murmur. Subsequently her physical capacity decreased progressively. She became breathless when she climbed five or six steps. During the past year, even walking on a level surface was poorly tolerated. When the patient walked just one block, she gasped for air, and, if she did not rest for awhile, she felt like fainting. Once while walking pulmonary edema with bloody sputum developed. In February, 1952, swelling of the ankles was observed. In September, 1952, the heart action became irregular.

Physical examination revealed a well-developed woman who did not appear severly ill. Cyanosis, dyspnea, and edema were absent. The cervical veins were not distended but filled during systole and collapsed during diastole. The lungs were clear. An apical thrust of the heart was not felt. During systole, a heaving pulsation of marked intensity was seen and felt in the precordial area. It extended between the third and fifth interspaces from the left parasternal line as far as 1 cm. beyond the left midclavicular line. Auscultation in the apical region revealed a snapping first and a loud second sound and a rumbling diastolic murmur. More medially, a soft blowing systolic murmur was heard. The second pulmonic sound was greatly accentuated. The heart rate was 80 per minute. The blood pressure was 135/95 mm. Hg. There was no evidence of congestive heart failure. The pulsation of the precordial area was recorded by means of the Cambridge mechanical transducer. The graph shown in figure 1 was taken with the receiver, a small funnel, placed in the fourth intercostal space in the left parasternal line. The tracing rises about 0.04 of a second after the onset of QRS and forms a plateau similar to the elevation felt during systole.

Roentgenologic study showed marked enlargement of the heart, especially of the right ventricle. The outflow tract of the left ventricle appeared to be elongated. The left atrium was moderately dilated. The pulmonary artery segment was prominent, and the hilar shadows were enlarged. Examination in the lateral view showed that the enlarged right ventricle was in broad contact with the anterior thoracic wall. An electrocardiogram demonstrated atrial flutter, marked right axis deviation, and prominent R deflections in the right precordial leads. The clinical diagnosis was tight mitral stenosis, probably associated with slight mitral regurgitation.

Mitral commissurotomy was performed on Oct. 15, 1952. The mitral orifice was tight and admitted no more than the tip of the index finger. There was minimal mitral regurgitation.

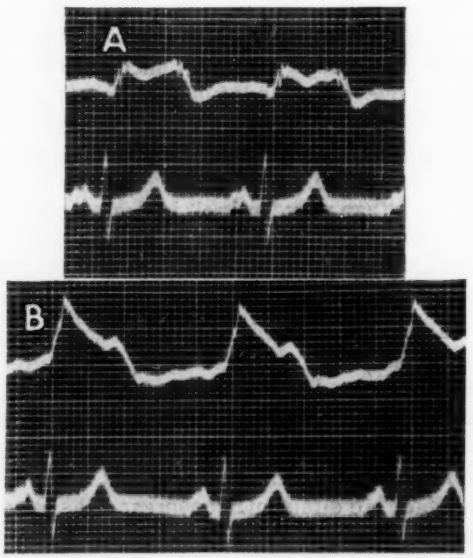

Fig. 2.—Upper tracings in both graphs represent displacement curves of the precordium taken in the fourth intercostal space, *A*, in the left parasternal line and, *B*, in the left midclavicular line. Electrocardiograms below.

Finger fracture of the fused commissures was easily performed. The patient made an uneventful recovery, and, seven weeks after the operation, she reported that her capacity for effort had markedly increased.

CASE 2.—A 28-year-old housewife was admitted to the hospital on July 27, 1952. She had had chorea at the age of nine. At that time, a heart murmur was said to be present. Subsequently the patient tired easily and often complained of muscle pain in the extremities. She married at the age of 22 and delivered a healthy child two years later. During labor, acute pulmonary edema developed. After pregnancy, the patient's condition progressively deteriorated. She felt weak and could

2. Dressler, W.: Pulsations of the Wall of the Chest: General Consideration, Arch. Int. Med. **60**: 225 (Aug.) 1937. Dressler, W.: Symposium on Cardiovascular Diseases: Cardiac Diagnosis Without Laboratory Aid: Pulsation and Percussion Signs, M. Clin. North America **34**: 721 (May) 1950.

3. Viar, W. N., and Harrison, T. H.: Chest Pain in Association with Pulmonary Hypertension: Its Similarity to Pain of Coronary Disease, Circulation **5**: 1 (Jan.) 1952.

4. Dressler, W.: Pulsations of the Wall of the Chest: Pulsations Associated with Tricuspid Regurgitation, Arch. Int. Med. **60**: 441 (Sept.) 1937.

scarcely do her housework. In the past two years, she could walk no more than one short block. When she forced herself to walk further, she became breathless, started to cough, and, on occasions, felt severe pain in the chest and back.

Physical examination showed a well-developed woman who did not appear to be seriously ill. She could lie flat in bed without experiencing shortness of breath. Cyanosis and edema were absent. The lungs were clear. The apical thrust of the heart was felt in the fifth intercostal space in the left midclavicular line. It had a "snappy" quality and was neither broad nor heaving. In the precordial area, a heaving pulsation could be seen and felt. It extended between the third and sixth ribs from the left sternal margin to the left midclavicular line. Auscultation in the apical area revealed a presystolic murmur,

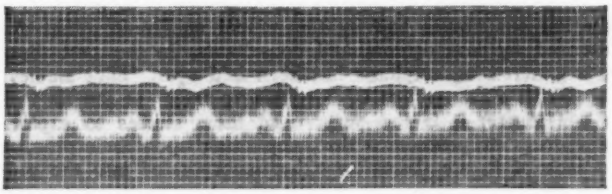

Fig. 3.—In patient with mitral stenosis, symptoms and signs point to a valve lesion of mild degree. The upper tracing represents displacement curve of the precordium taken from the fifth intercostal space in the left parasternal line; shallow depression is seen during systole. Electrocardiogram below.

a loud first sound, and a prolonged diastolic rumble. Similar findings of lesser intensity were heard close to the sternum. The second pulmonic sound was greatly accentuated. The heart rhythm was regular, and the rate was 72 per minute. The blood pressure was 110/70 mm. Hg.

The precordial pulsation was taken from the fourth intercostal space (fig. 2), in the left parasternal line, and in the left midclavicular line. In both graphs, the tracing rises early in systole and forms a plateau similar to the elevation felt during systole. Roentgenologic study indicated a moderately enlarged heart with a flattened left border. The left atrium was dilated. The right lateral view showed fulness of the cardiac shadow anteriorly, close to the sternum, that was thought to be due to enlargement of the right ventricle. An electrocardiogram showed regular sinus rhythm, signs suggestive of atrial hypertrophy, and semivertical electrical position of the heart.

Commissurotomy was performed on Aug. 4, 1952. The mitral valve was tightly stenotic and admitted no more than the tip of the little finger. There was a slight regurgitating jet. Finger fracture of the calcified mitral ring was easily performed. The postoperative course was uneventful. When the patient was seen four months after operation, she expressed great satisfaction with the result. Her capacity for effort had increased greatly. She could climb two flights of stairs and do house work that she could not before because of marked dyspnea.

COMMENT

Normally, the precordial area over the right ventricle shows no heaving pulsation during systole. Sometimes, especially in young persons with flexible ribs, a slight depression is noted that is caused by the diminution of the cardiac volume.[2] Similarly, in instances of moderate mitral stenosis, the precordial area is either completely quiet or shows a slight pulsatory depression during systole. The complaints of a 48-year-old woman with mitral stenosis were mainly of nervous nature; her capacity for effort was nearly unlimited. None of the signs pointed to tight mitral stenosis. The graph (fig. 3) was taken from the fifth intercostal space in the left parasternal line. Instead of a plateau elevation, as shown in figures 1 and 2, a shallow depression was noted during systole.

In patients with mitral stenosis, a heaving pulsation is frequently observed during systole in the precordial area over the right ventricle. The displacement is usually most marked in that part of the precordium adjacent to the left sternal margin between the third and sixth ribs. The pulsation may sometimes extend over the lower half of the sternum and slightly beyond the right sternal margin; caudally, it may reach the left costal arch. Occasionally, when the outflow tract of the greatly enlarged right ventricle has shifted considerably to the left, the heaving pulsation is most pronounced in the left midclavicular line.

It should be stressed that the precordial pulsation can be recognized without the aid of graphs merely by inspection and palpation. Sometimes, when the displacement is marked, the chest piece of the stethoscope resting on the precordium can be seen to be lifted with each systole. In all instances, the pulsation is easily recognized by palpation. It is best felt when the examiner, standing to the patient's right, applies the carpal base of his right hand with considerable pressure to the precordial area close to the lower half of the sternum.

Johnston and Overy [5] obtained, with an electric transducer, displacement curves from the precordial region close to the left sternal edge that showed "prominent upward waves in systole" in patients with mitral stenosis. They suggested that systolic distension of a large right atrium resulting from tricuspid regurgitation rather than right ventricular hypertrophy was responsible for the precordial pulsation. This interpretation is at variance with our experience. Tricuspid regurgitation, when marked, tends to cause a depression of the precordial area because of the marked diminution in the volume of the right ventricle.[4] Figure 4 shows graphs that were obtained from a 47-year-old patient who was operated on for tight mitral stenosis. An associated tricuspid regurgitation was

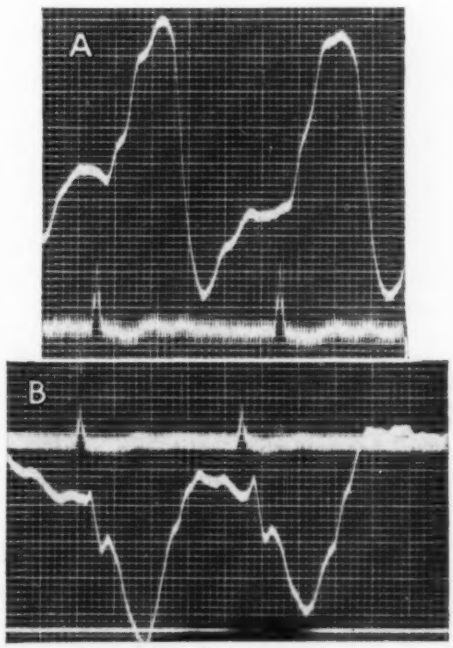

Fig. 4.—In patient with tight mitral stenosis and marked tricuspid regurgitation, *A*, upper graph of liver pulse shows marked elevation during systole; electrocardiogram below. *B*, lower graph taken over the fourth interspace in the left midclavicular line shows a distinct depression during systole; electrocardiogram above.

5. Johnston, F. D., and Overy, D. C.: Vibrations of Low Frequency over the Precordium, Circulation 3: 579 (April) 1951.

revealed by observation of an expansile systolic pulsation of the liver and the cervical veins. Graph *A*, taken from the liver, shows a marked systolic upward wave. Graph *B*, taken from the fourth interspace in the left midclavicular line, demonstrates a depression of the precordium during systole.

SUMMARY AND CONCLUSIONS

A physical sign associated with tight mitral stenosis is described. It is characterized by a heaving pulsation during systole of the precordial area over the right ventricle. The pulsation is caused by the forceful action of a markedly enlarged right ventricle. Dilatation of the left atrium that forces the heart toward the anterior chest wall is probably a contributing factor. Correlation of the precordial pulsation with observations made during surgery indicates that displacement caused by pulsation is associated with tight mitral stenosis. The sign has proved to be a useful aid in the selection of patients for commissurotomy.

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COUNCIL ON PHARMACY AND CHEMISTRY

REPORT TO THE COUNCIL

The following paper, prepared by Nicholas D'Esopo, M.D., of the Veterans Administration Hospital, West Haven, Conn., is the fifth in a series of progress reports on the cooperative investigation of the chemotherapy of tuberculosis that was initiated by the Veterans Administration, Army, and Navy in May, 1946. The report immediately preceding this described the situation as it existed at the time of the Tenth Conference on the Chemotherapy of Tuberculosis, in January, 1951; the present report is designed to cover the two year interval between that date and the Twelfth Conference, held in February, 1953. The number of cooperating hospitals has remained substantially unchanged at 50 but, during this interval, the number of cases reported has increased from 10,000 to approximately 15,000.

The Council has authorized publication of this report.

R. T. STORMONT, M.D., *Secretary.*

CHEMOTHERAPY OF TUBERCULOSIS IN MAN

PRESENT STATUS

The mechanics of the study of the chemotherapy of tuberculosis by the Veterans Administration, Army, and Navy have been described in previous reports [1] and are reviewed briefly here. The cooperating hospitals developed, and repeatedly revised, a series of protocols that dealt with such matters as diagnostic criteria, regimens, and laboratory procedures. The primary purpose has been to compare the efficacy of a series of chemotherapeutic regimens, the relative values of which were unknown at the time the comparisons were initiated. The patients have been divided among these regimens by random allocation on the basis of their hospital registration number. Individual case report forms, which permit the collection and analysis of data for consideration by the periodic conferences, are utilized. The criteria of efficacy have gradually been limited to the objective observations of sputum conversion and radiological change. Adjuvant therapy in the form of bed rest has been continued without substantial change since 1946 and, in the form of pulmonary resection or collapse, has been employed at the discretion of the investigators since the fall of 1947. Liaison has been maintained by the prompt circulation of informal progress reports to which each hospital contributes and by the annual conferences that are attended by investigators and consultants. In the past three years, increasing emphasis has been laid upon "pilot studies" for which small groups of hospitals volunteer at the time of a conference; it is the purpose of these studies to explore new drugs or procedures that, depending upon their promise or lack of it, are thereafter either incorporated into the general study for a broader examination or are rejected.

The course that the study pursued can be tersely summarized as follows: After the usefulness of streptomycin was established (1946-1947), changes in dosage and in the duration of treatment were explored (1947-1949) in an attempt to enhance that usefulness and to circumvent the disadvantages of the drug's toxicity and the resistance that tubercle bacilli developed to it. Subsequently, the study proceeded (1949-1952) to investigate the newer chemotherapeutic agents and is now proposing to evaluate certain adjuvant measures, such as pneumoperitoneum, when given in conjunction with prolonged chemotherapy.

A study of this kind has numerous obvious advantages and disadvantages. Chief among the advantages is the rapidity with which large masses of data can be gathered, a point of particular value in such a chronic and protean disease as tuberculosis; chief among the disadvantages is the large number of workers (quite literally, hundreds) who participate in the study, with the consequence that the incomplete or inaccurate work of a few dilutes the accuracy of the work of the many.

For the purposes of the present report, it has seemed best not to present figures and tables similar to those employed in preceding reports but rather to discuss the present status of the chemotherapy of tuberculosis in a broader and more narrative fashion. This is made possible by the fact that, although many problems remain to be solved, there is now a vast amount of data and a great degree of agreement on certain fundamental principles of chemotherapy in this field. This agreement even extends to the similar studies, formulated somewhat later, by the U. S. Public Health Service and the Medical Research Council of Great Britain.[2b] (The similarities between the protocols adopted by these three groups are quite astonishing, indicating, perhaps, that they are the best that can be expected.) It would appear that the time is approaching when it will be feasible to delegate to the general practitioner certain phases of the treatment of tuberculosis now undertaken only by the phthisiologist. This report is primarily directed to these nonspecialists and will be concerned almost exclusively with pulmonary tuberculosis. First discussed is the present standing of individual drugs and their regimens; a discussion of more general topics follows.

INDIVIDUAL DRUGS AND DRUG REGIMENS

Streptomycin and p-*Aminosalicylic Acid.*—Since 1949, streptomycin has been administered to patients only in combination with some other antituberculosis agent. The oldest of these combined regimens is that employing *p*-aminosalicylic acid. The greater part of our knowledge of combined therapy in tuberculosis has come from experience with this regimen. In the beginning, 1 gm. of streptomycin was used daily with 12 gm. of *p*-aminosalicylic acid daily. In 1950, the regimen consisting of 1 gm. of streptomycin given twice weekly and 12 gm. of *p*-aminosalicylic acid daily was explored. In Janu-

Prepared at the request of the Twelfth Veterans Administration-Army-Navy Conference on the Chemotherapy of Tuberculosis, Atlanta, Ga., Feb. 9-12, 1953.

1. Reports to the Council on Pharmacy and Chemistry: (*a*) Effects of Streptomycin on Tuberculosis in Man, J. A. M. A. **135**: 634 (Nov. 8) 1947; (*b*) Streptomycin in Treatment of Tuberculosis: Current Status, ibid. **138**: 584 (Oct. 23) 1948; (*c*) Current Status of Chemotherapy of Tuberculosis in Man: A Summary Report, ibid. **142**: 650 (March 4) 1950; (*d*) Chemotherapy of Tuberculosis in Man: Present Status, ibid. **147**: 253 (Sept. 15) 1951.

2. (*a*) Transactions of the Tenth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D. C., Jan., 1951. (*b*) Transactions of the Eleventh Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D. C., Jan., 1952. (*c*) Transactions of the Twelfth Conference on the Chemotherapy of Tuberculosis, Veterans Administration, Washington, D. C., Feb., 1953.

ary, 1952, this regimen had all but replaced that of daily administration of streptomycin. A large number of patients have now been treated by both the daily streptomycin and twice-weekly streptomycin regimens; statistical analysis indicates that they are quite similar in therapeutic efficacy. In patients receiving their first course of chemotherapy, the incidence of sputum conversion during treatment with either of the two regimens after the eighth month is in the range of 60 to 80%, and moderate to marked improvement as shown by roentgenography occurs in approximately 80%. Unfavorable changes in roentgenograms during therapy are uncommon, probably in the order of 5 to 10%. The protocols under which these studies are made permit any form of adjuvant therapy to be employed during chemotherapy; however, analysis of the "background" data suggests that collapse therapy and surgery were used with approximately equal frequency in both groups of patients.

While use of streptomycin twice weekly and *p*-aminosalicylic acid daily is now considered the regimen of choice by most, a few investigators assert that some patients do better if they are treated with streptomycin daily. They believe that it is probably incorrect to attempt to decide upon a single streptomycin-*p*-aminosalicylic acid regimen that will be suitable for all cases and that patients with small lesions, for example, may do quite as well with streptomycin twice weekly as with the daily regimen, whereas patients with large cavities may require streptomycin daily. It is hoped that a more detailed analysis of the large amount of statistical material in the possession of the study may supply the answer to this question.

Abundant evidence indicates that bacterial sensitivity to streptomycin is better maintained with the twice weekly streptomycin regimen than with the daily; however, other data suggest that streptomycin twice weekly is not always sufficient to preserve bacterial sensitivity to *p*-aminosalicylic acid. This is another point that may be resolved by a more careful analysis of data already at hand.

Combined streptomycin and *p*-aminosalicylic acid therapy has been used for almost five years, and much has been learned about the efficacy and toxicity of this regimen. To many clinicians, this regimen is synonymous with the chemotherapy of tuberculosis; its therapeutic effect has become more or less predictable to the experienced. The influence of this experience may have the disadvantage of delaying acceptance of potent, new agents, and, in some instances, may actually impede the investigation of minor drugs that might prove to be of value. On the other hand, it lessens the risk of assuming that a new regimen, such as streptomycin and isoniazid combined, possesses all the qualities that have come to be associated with combined streptomycin and *p*-aminosalicylic acid therapy before actual experience with the newer regimen is worked out. The average physician should probably depend upon a tried regimen like streptomycin and *p*-aminosalicylic acid combined until other regimens have been proved to be superior in adequate clinical trials. The use of streptomycin and isoniazid combined as the initial chemotherapy of pulmonary tuberculosis entails the risk of bacterial resistance to the only two really effective antituberculosis drugs in use. Whether this combination of two major agents has a distinct advantage over a combination of a major agent (streptomycin) and a minor agent (*p*-aminosalicylic acid) must be determined.

The practice of prescribing *p*-aminosalicylic acid alone is probably uncommon at the present time in this country. It bears mention only because it is to be avoided. Tubercle bacilli often become resistant to the drug. When this occurs, it loses its ability to delay or prevent resistance to streptomycin if it is used later in combination with that drug. It is paradoxical that *p*-aminosalicylic acid, itself an extremely weak chemotherapeutic agent, allows the almost unlimited prolongation of streptomycin therapy when both drugs are used together.

The optimum dosage of *p*-aminosalicylic acid used in combination with streptomycin is not known. A few data suggest that doses of 5 to 10 gm. per day are less effective in preserving sensitivity to streptomycin in combined therapy than larger doses, such as 20 gm. daily.[3] It is well to remember that the dose commonly employed, 12 gm. per day, is simply the largest dose tolerated by the average patient. This dose, however, has the sanction of experience; in the majority of cases it does delay or prevent development of resistance to streptomycin. Hence, it would seem wise for the physician to adhere as closely as possible to this daily dose, with an awareness of the possibility that doses below this amount may be ineffective in preventing resistance to streptomycin.

In computing and reporting the dosage of *p*-aminosalicylic acid it should be remembered that its salts weigh considerably more than the free acid. Thus, 16.5 gm. of sodium *p*-aminosalicylate contains only 12 gm. of the acid, and similarly 12 gm. of sodium *p*-aminosalicylate contains approximately 8.7 gm. of acid. To state amounts in terms of the salts is misleading; it is suggested that the dosage be referred to in terms of the free acid, the active form of the drug.

The occurrence of sensitivity reactions in patients receiving *p*-aminosalicylic acid is well known. The peak incidence is toward the end of the first month of therapy. Patients have the usual characteristics of sensitivity phenomena, which appear abruptly with fever, skin rash, and constitutional symptoms of varying severity. It is absolutely mandatory that use of the drug be discontinued when these reactions occur. Until isoniazid became available, it was necessary to "desensitize" patients in whom such reactions occurred by using small, gradually increasing amounts of the drug. Frequently this required two months to accomplish, and much time was lost in consequence. Now, it hardly seems necessary to attempt to desensitize these patients, as isoniazid almost always can be substituted with a delay of only several days.

Dihydrostreptomycin.—After a considerable experience in which the effectiveness and toxicity of dihydrostreptomycin were compared with that of streptomycin, the cooperating hospitals discontinued any general use of the former drug in 1950. Since that time there has been no reason to reinstate it. Experience has reaffirmed the earlier conclusions that this reduction product of streptomycin causes appreciably more deafness than the parent drug.[4] In a dosage of 1 gm. daily, this toxicity does not become apparent until the drug is given for more than four to six months. For this reason, studies in which patients have been treated with dihydrostreptomycin for only four months are apt to give an inaccurate idea of its potential toxicity, especially now that there is a tendency toward the use of much longer courses of chemotherapy. It should be pointed out that the vestibular and auditory toxicity of either streptomycin or dihydrostreptomycin is appreciably diminished in the twice-weekly regimens.

At present the chief advantage of dihydrostreptomycin appears to be its use for those patients, usually in the older age group, whose vestibular mechanism is peculiarly susceptible to streptomycin. It is also of value for patients who are allergic to streptomycin. A combination of dihydrostreptomycin and streptomycin, using half the usual quantities of each drug, is currently being investigated; its purpose is to diminish or prevent both auditory and vestibular toxicity without affecting therapeutic efficacy. Results are said to be promising, but studies of prolonged administration have not yet been reported.[2c]

Isoniazid.—Isoniazid became available to the medical profession in May, 1952. Considerable experience with it has now accumulated since the pilot studies were begun by the Veterans Administration, Army, and Navy group in early February, 1952. The effectiveness of a daily dose of 0.15 gm. was compared with that of 0.3 gm. and with the "standard" regimen of streptomycin and *p*-aminosalicylic acid combined. The results of these trials,[2c] in general, supported the first reports that indicated that isoniazid was an antituberculosis agent of great potency, but were certainly not as striking as those reported by the original investigators. This discrepancy may be explained, at least in part, by the fact that many of the patients in the original studies were treated with the isopropyl derivative of isoniazid, iproniazid, which often causes spectacular symptomatic improvement and weight gain. The

3. Prevention of Streptomycin Resistance by Combined Chemotherapy: A Medical Research Council Investigation, Brit. M. J. 1: 1157 (May 31) 1952.

4. O'Connor, J. B.; Christie, F. J., and Howlett, K. S., Jr.: Neurotoxicity of Dihydrostreptomycin, Am. Rev. Tuberc. 63: 312 (March) 1951. Footnotes 2a and 2c.

clinical trials in our hospitals made it clear that isoniazid, by itself, resulted in great symptomatic benefit to the patient, but those roentgenographic and bacteriological changes that lead to cure, or even arrest, of the disease often did not occur. In the majority of the patients treated with isoniazid alone, isoniazid-resistant bacilli could be recovered after the second month of treatment. When bacterial resistance to a drug occurs, the assumption that continued treatment with that drug will not be effective is justified. This was certainly true of streptomycin.

The situation with isoniazid appears to be somewhat different. In a seminar at the Twelfth Conference (February, 1953),[2e] it was reported that, while patients often fail to improve further when bacterial resistance to isoniazid develops, they often maintain clinical improvement made before bacterial resistance occurred—sometimes in the face of unfavorable roentgenographic changes. This relative lack of correlation between resistance to isoniazid and the clinical condition of the patient may be related to the virulence of isoniazid-resistant tubercle bacilli—a matter that is now receiving wide notice. Several investigators reported that isoniazid-resistant bacilli are often avirulent: they fail to cause tuberculous infection when injected into susceptible experimental animals.[2e] This phenomenon is quite variable; the frequency with which it occurs is not yet known, but it is by no means uncommon. Obviously, there is much speculation on the practical significance of this laboratory finding in the treatment of human tuberculosis. At the present time its significance is not known. Patients who are doing poorly clinically and becoming progressively worse may harbor isoniazid-resistant bacilli that are not virulent for guinea pigs. The opposite is also true; patients who show progressive improvement on isoniazid therapy may discharge bacilli that are quite virulent. Until this phenomenon is better understood, it would seem best to completely disregard it in clinical practice; every effort should be made to prevent the development of isoniazid-resistant bacilli.

In 1952, the cooperating hospitals undertook a study of the comparative efficacy of streptomycin combined with *p*-aminosalicylic acid as compared to streptomycin combined with isoniazid and to isoniazid combined with *p*-aminosalicylic acid, the streptomycin being administered twice weekly in the two regimens containing it. Preliminary data on this point compiled for the Twelfth Conference suggest that these regimens are of equal therapeutic value when efficacy is measured by serial x-ray changes and sputum conversion. As far as toxicity is concerned, nothing thus far indicates that 0.3 gm. of isoniazid daily may not be administered safely for long periods of time. Nevertheless, it must be borne in mind that sufficient data on the toxicity of polonged isoniazid administration are lacking. Possibly because of the manner in which isoniazid was introduced to the medical profession (via the newspaper), it has been too readily assumed that a combination of streptomycin and isoniazid is therapeutically superior to combined streptomycin and *p*-aminosalicylic acid. There is no evidence for this assumption.

The relative efficacy of daily administration of streptomycin and daily administration of isoniazid as compared with twice weekly administration of streptomycin and daily administration of isoniazid is not known. At the Twelfth Conference, a pilot study was drawn up to compare these regimens; this was begun in March, 1953. Studies were also begun to compare a combination of streptomycin, isoniazid, and *p*-aminosalicylic acid with regimens employing only two of these three drugs, that is, streptomycin plus isoniazid, streptomycin plus *p*-aminosalicylic acid, or isoniazid plus *p*-aminosalicylic acid.

The toxic manifestations of isoniazid are many, though few of them are important. They are said to occur in about 5% of the patients treated and to necessitate cessation of treatment in about 1%. The isopropyl derivative, iproniazid, is so much more toxic than the parent compound that it has never been available except for investigative purposes. Its use may be followed by withdrawal symptoms. The toxic manifestations mentioned subsequently are those of isoniazid and have been noted with doses of 0.15 to 0.3 gm. per day. At some point above this level, probably in the range of 0.45 to 0.6 gm., all toxic reactions can be expected to occur more frequently. The nervous system is involved most frequently, the commonest symptoms being twitching of muscles, restlessness, insomnia, and headache; hyper-reflexia can often be demonstrated. These toxic reactions disappear when the drug is withdrawn and often even if it is continued; they are rarely important enough to interfere with therapy. In some patients there are changes in temperament, at times characterized by irritability or euphoria, that are very difficult to evaluate, especially since these patients have often displayed a somewhat similar behavior before chemotherapy. These subtle changes in personality may indeed be the commonest toxic manifestations of all. A considerable number of patients experience an increase in libido and have frequent erections and nocturnal emissions. Much more important manifestations of central nervous system toxicity, but much less common, are convulsions, psychoses, and difficulty in micturition. Convulsions and psychoses are said to be more frequent in patients with organic brain damage and in those with unstable personalities.

The allergic reactions to isoniazid are not distinctive and are relatively infrequent. Desensitization by the administration of small, gradually increasing doses is said to be successful. Reports of severe reactions during isoniazid therapy are so few in number that it is impossible to attribute them with certainty to the drug. These include purpura, jaundice, and agranulocytosis. More observations on these points are needed.

At present it is agreed that isoniazid should not be used alone in the treatment of pulmonary tuberculosis, but it is not known whether streptomycin and isoniazid combined are preferable to streptomycin and *p*-aminosalicylic acid combined in the treatment of a patient who never before has received antituberculosis drugs, that is, in one whose bacilli are not resistant to any of these three drugs. The combined streptomycin and *p*-aminosalicylic acid regimen is better known and better established. The combined streptomycin and isoniazid regimen gives promise of being equally as effective as the streptomycin and *p*-aminosalicylic acid regimen, but this has not yet been clearly established. In the Veterans Administration, Army, Navy group, the 1952 pilot study comparing use of streptomycin and *p*-aminosalicylic acid, streptomycin and isoniazid, and isoniazid and *p*-aminosalicylic acid is being continued as a "basic" study; other controlled clinical studies are also in progress. It is hoped that a conclusive answer to this question will soon be forthcoming.

Oxytetracycline (Terramycin) and Viomycin.—Two derivatives of the genus Streptomyces, oxytetracycline (Terramycin) and viomycin, deserve mention as potentially valuable drugs in the treatment of tuberculosis. The antituberculosis activity of oxytetracycline, a broad-spectrum antibiotic derived from Streptomyces rimosus, was first investigated by the study units in 1950. This antibiotic inhibits the growth of tubercle bacilli in a concentration of 4 to 16 mcg. per milliliter in vitro. It is also active against tubercle bacilli resistant to streptomycin and to other tuberculostatic drugs. When streptomycin and *p*-aminosalicylic acid were the only effective antimicrobial agents available for the treatment of tuberculosis, it seemed reasonable to assess the value of oxytetracycline in limited clinical trials. The results of these trials have not been conclusive. The only enthusiastic report was that of the Fitzsimons Army Hospital; studies carried out in several Veterans Administration Hospitals were disappointing.[2a] The discrepancies in these studies in part may have resulted from the more favorable variety of clinical material in the Fitzsimons study (recently discovered lesions in young men) in addition to the much greater tolerance of their patients to oxytetracycline (7 gm. per day). This extraordinary tolerance could not be duplicated elsewhere, and, indeed, the financial expense of such therapy would appear to be prohibitive. Since the advent of isoniazid, there have been no further reports of studies on the efficacy of oxytetracycline as a sole agent in the treatment of tuberculosis. At the moment the data are incomplete, but it is probably fair to assume that for the average patient receiving average doses (2 to 3 gm. per day), its efficacy is of a low order. On the other hand, it is entirely possible that for a patient tolerating unusually high dosages the drug may be quite effective, as the experience at Fitzsimons suggests.

Probably more important than the clinical trials with oxytetracycline as the sole drug are the studies of its use in combination with streptomycin. Under these circumstances, there is ready agreement that it is effective in delaying or preventing the emergence of resistance to streptomycin—a really noteworthy contribution because of the large number of patients whose bacilli become resistant to *p*-aminosalicylic acid following therapy with that drug. The regimen consisting of 5 gm. of oxytetracycline daily and 2 gm. of streptomycin every third day, which was investigated by the Fitzsimons Group, has resulted in the preservation of sensitivity to streptomycin in every one of 15 patients whose cultures were still positive after 120 days of therapy.[2b] The regimen of 5 gm. of oxytetracycline daily and 1 gm. of streptomycin twice weekly, employed by the Veterans Administration Hospital at Dayton, Ohio, yielded approximately the same results.[2b] More recent reports from several clinics suggest that 2 gm. per day is similarly effective in this respect, and some evidence suggests that 1 gm. daily may produce the same result.

The tubercle bacilli of a large number of patients have become resistant to both streptomycin and *p*-aminosalicylic acid during successive courses of treatment with these drugs. If these patients were now treated with isoniazid, the risk of developing bacilli that are also resistant to this drug would be great, even if it were used in combination with streptomycin or *p*-aminosalicylic acid. For this group of patients, a combination of isoniazid and some other antituberculosis drug to which tubercle bacilli are still sensitive is required. It is hoped that oxytetracycline may fill this need by preserving sensitivity to isoniazid as effectively as it does to streptomycin. Studies on this point are now in progress.

Viomycin has also recently become available for clinical use. This antibiotic, derived from Streptomyces puniceus and Streptomyces floridae, is active in vitro against both streptomycin-sensitive and streptomycin-resistant bacilli in concentrations of 2.5 to 12.5 mcg. per milliliter. Tubercle bacilli become resistant to viomycin in vitro and in patients treated with it. In experimental animals, it is approximately 25% as effective as streptomycin in equivalent dosage.[5]

The first clinical trials of viomycin were carried out with a dosage approximating 50 mg. per kilogram of body weight (2.5 to 3.5 gm. per day). In these trials,[6] the therapeutic efficacy of the drug was appreciable though it seemed definitely inferior to streptomycin. It is difficult to make such a quantitative comparison between the two drugs with any precision, especially since, within the ranges tolerated by human beings, the efficacy of viomycin appears to be more a function of dosage than it is with streptomycin. Patients who tolerate 3 gm. per day have often showed striking improvement of pulmonary and extrapulmonary lesions; however, this dosage causes serious toxic reactions, chiefly albuminuria, azotemia, hypokalemia, and hearing loss that may be sudden and complete. Patients who do tolerate this dose of the drug often require a prohibitive amount of laboratory work for detection and control of toxic manifestations.

Because of its toxicity, recent clinical studies have been carried out with a regimen of 2 gm. of viomycin twice weekly and 12 gm. of *p*-aminosalicylic acid daily, a considerable reduction in dosage as compared to the first trials. At this dosage,[2b,c] the toxicity is sharply reduced and yet the difference is quantitative; all toxic manifestations observed with the higher dosages continue to occur and should be anticipated. The therapeutic efficacy of this regimen is moderate, but it is not yet possible to know what may be expected of it in terms of the significant therapeutic goals in pulmonary tuberculosis, that is, sputum conversion and cavity closure, nor has its preoperative prophylactic value been defined. A large number of patients have been treated with this regimen in both Veterans Administration and non-Veterans Administration hospitals. An analysis of these data will be available soon. At present the place of viomycin among the antituberculosis drugs is uncertain. Because of its limited efficacy and toxicity, it is evident that viomycin seldom will be the drug of choice. As is the fate of less effective drugs, it will probably be used in the treatment of those patients whose bacilli have become resistant to streptomycin or isoniazid. For such use, it will probably be of value, but it should be used in the proper setting, with facilities for careful laboratory control of toxicity.

Amithiozone (Tibione), Pyrazinamide (Aldinamide), and Certain Antibiotics.—The position of amithiozone (Tibione), one of the thiosemicarbizones, among antituberculosis drugs has now been clearly defined; its efficacy, though often discernible, is not usually sufficient to alter the patient's therapeutic problem or contribute significantly to his recovery. According to most investigators, its efficacy is approximately that of *p*-aminosalicylic acid. At the present time there appears to be no place for the thiosemicarbizones in the treatment of pulmonary tuberculosis except possibly as a last resort in patients who have failed utterly to respond to all other antituberculosis drugs. Whether or not the thiosemicarbizones should be administered in combination with other drugs is doubtful. The matter has not been studied sufficiently; the data are conflicting.

Some reports indicate that amithiozone may be of benefit in lesions of the mucous membrane; patients whose bacilli were resistant to streptomycin have experienced significant relief of laryngeal lesions and tuberculous enteritis. The drug is worth remembering for this indication alone.

The clinical usefulness of the thiosemicarbizones is limited by their toxicity; in experimental tuberculosis, excellent therapeutic results have been obtained with dosages that would be equivalent to 3 gm. per day in man, but amounts of that order are absolutely precluded by toxicity. Dosages of 0.1 to 0.2 gm. per day are well tolerated. In this range toxicity is minimal and reversible when it occurs. Larger doses (0.2 to 0.8 gm. per day) are probably not significantly more effective and are considerably more toxic.

Pyrazinamide (Aldinamide), a synthetic derivative of nicotinic acid, was first used in tuberculosis in clinical trials in 1949. In the few studies that have been made with it, the immediate therapeutic effect of the drug is frequently striking. Many patients experience an abrupt defervescence and, often, pronounced symptomatic improvement.[7] Roentgenograms reveal appreciable and sometimes almost complete resolution of lesions. Laryngeal and palatal lesions have healed in several instances. Its value, however, appears to be limited to recent cases with fresh, exudative lesions, and its effectiveness even in these favorable cases is short lived. This loss of efficacy is ascribed to the rapid development of bacterial resistance—a point, however, that should not interfere with its usefulness as a prophylactic agent in thoracic surgery. Toxic manifestations noted in patients treated with 2.8 gm. per day consist of nausea, vomiting, arthralgia, fever, nervousness, and jaundice. These are reversible on withdrawal of the drug.

A brief experience with pyrazinamide has not impressed the investigators in the cooperating hospitals, although a few of them believe that its study should be continued. This attitude can be readily understood, for it is difficult to abandon entirely a drug that often gives striking relief, even though briefly, to patients with acute disease. No doubt the study of pyrazinamide on a larger scale would be desirable, but the presence of much more powerful competitors in the field makes this course improbable at the moment.

A host of other synthetic chemical compounds—most of them modifications of isoniazid—are receiving extensive laboratory trials; some are already receiving clinical trials, but none are sufficiently developed to deserve mention at this time. Their stature probably will be that of secondary weapons—substitutes for streptomycin and isoniazid when tubercle bacilli become resistant to these drugs.

Three antibiotics, in addition to those already mentioned, have been discussed at the conferences but have not succeeded in holding attention. Neomycin,[2a] an admirable performer in the laboratory, exerts too toxic an effect upon the kidney and

5. Steenken, W., Jr., and Wolinsky, E.: Viomycin in Experimental Tuberculosis, Am. Rev. Tuberc. **63**: 30 (Jan.) 1951.

6. Werner, C. A.; Tompsett, R.; Muschenheim, C., and McDermott, W.: Toxicity of Viomycin in Humans, Am. Rev. Tuberc. **63**: 49 (Jan.) 1951. Footnote 2a.

7. Yeager, R. L.; Munroe, W. G. C., and Dessau, F. I.: Pyrazinamide (Aldinamide) in the Treatment of Pulmonary Tuberculosis, Am. Rev. Tuberc. **65**: 523 (May) 1952.

the auditory branch of the eighth cranial nerve to justify its clinical use except possibly as a local application (such as for tuberculous cystitis). Mycomycin,[2a,b] finally obtained after heroic efforts to stabilize it, proved practically inactive in the treatment of tuberculous guinea pigs. Erythromycin has received a small-scale clinical trial and, as might have been anticipated from in vitro studies, was found to be ineffective.[2c]

OTHER ASPECTS OF CHEMOTHERAPY

Optimum Duration.—The chronicity of tuberculosis and the frequency with which necrotic lesions are present suggest that long periods of bacterial suppression are required before lasting healing can be expected. Certainly this is true as long as the available chemotherapeutic agents merely inhibit the growth of tubercle bacilli rather than directly destroy them. The present group of antituberculosis drugs are tuberculostatic rather than tuberculocidal, and the optimum duration of chemotherapy must be discussed with this point in mind.

The earliest studies of streptomycin pointed to the development of streptomycin-resistant bacilli as the major obstacle to effective, prolonged chemotherapy. Once resistant bacilli appeared, further therapy was usually without benefit and relapses were frequent. This was changed by administering streptomycin in combination with *p*-aminosalicylic acid. The addition of *p*-aminosalicylic acid to the regimen has significantly delayed or even suppressed the emergence of streptomycin-resistant bacilli, and this has made prolonged streptomycin therapy possible. In 1949, at the Eighth Conference, the report of a pilot study conducted by a single hospital suggested the superior effectiveness of prolonged streptomycin and *p*-aminosalicylic acid therapy over the 120-day regimens then in use.[8] In 1950, at the Ninth Conference, the principle of prolonged chemotherapy was incorporated into the basic regimens that were to be used by all cooperating hospitals.

In the protocols agreed upon at this time, however, the duration of a course of combined streptomycin and *p*-aminosalicylic acid therapy for the individual patient was left to the judgment of the investigator—it might be 4, 8, 12 or more months. The investigators were aware that in more advanced cases or those presenting difficult therapeutic problems treatment would be continued longer than in the more favorable cases and that, if the severity of the disease were not taken into account, it might appear that prolonged therapy was actually less effective than the shorter courses. Clearly, a controlled study was needed. Yet it never seemed wise to institute a strictly controlled study in which cases would be allocated at random at the start of chemotherapy. If this were done, a patient with minimal tuberculosis, for example, might fall by chance in the group to be treated for one year, while a patient with advanced disease might be treated for only four months. Studies on the duration of chemotherapy were discussed at successive conferences, but only at the most recent, in February, 1953, was a protocol for a pilot study on this subject proposed and accepted by the cooperating hospitals. The objection of allocating cases of varying severity at random was overcome by delaying selection until each case had attained a well-defined therapeutic goal. In the protocol recently adopted, this goal, the "therapeutic target point," consists of three parts: (1) the stability of lesions on serial roentgenograms, (2) the closure of all cavities, and (3) the finding of consistently negative cultures. When the target point is reached, whether by chemotherapy alone or by chemotherapy aided by adjuvant therapy (such as collapse or resection), random allocation in respect to the duration of chemotherapy is put into effect.

In order that the bacteriology and pathology of lesions at the time the target point is reached may be appreciated, the evolution of lesions during chemotherapy will be discussed briefly. The rapid clearing of x-ray shadows during the first three or four months of therapy represents chiefly the resolution of non-necrotic lesions. Further resolution then proceeds more slowly as chemotherapy is continued beyond the fourth or sixth month. Occasionally, steady resolution occurs throughout the entire first year of chemotherapy and even into the second year. At some time, varying widely in different cases, stability is reached and roentgenograms no longer show changes for the better. At this point of maximal resolution, most of the shadows that persist on the roentgenogram represent residual, necrotic lesions rather than scars.[2a] This fact cannot be overemphasized. These lesions are frequently encapsulated necrotic foci that never liquified and drained, and often they are cavities filled with necrotic debris.

The behavior of cavities during chemotherapy is probably the most important single criterion of the efficacy of a drug regimen. During the first several months of chemotherapy, cavities become reduced in size and small ones may close (or, rather, fill in). In general, however, closure of cavities lags behind the resolution of non-necrotic lesions. This lag was easily apparent during the 120 day courses of chemotherapy employed in our study prior to 1950; here the resolution of non-necrotic lesions was often pronounced, while the effect on cavities was meager. The infrequency of cavity closure led to the conclusion that chemotherapy had a beneficial effect upon "exudative disease" (non-necrotic) but not upon caseous lesions. During the relatively short courses of streptomycin therapy employed in those days, cavities often showed progressive reduction in size until such time as bacterial resistance was found in vitro, whereupon they frequently enlarged again. The impression was that some cavities would have closed completely if bacterial resistance had not supervened. This is precisely what does occur during prolonged therapy with combined streptomycin and *p*-aminosalicylic acid. A considerable number of cavities up to 6 cm. in diameter do close during chemotherapy without the aid of collapse measures. Most of the ones that close do so during the first six months; those that are still open at the sixth month require either collapse or resection to effect their closure or elimination.

The bacteriological changes during prolonged chemotherapy make up the third criterion of the therapeutic target point. In patients receiving combined streptomycin and *p*-aminosalicylic acid daily, approximately 75% have negative cultures at the end of the fourth month of their first course of uninterrupted therapy. Whether or not cultures will remain negative as chemotherapy is continued depends almost exclusively on the fate of cavities in each case. Some generalizations of great clinical usefulness are as follows: 1. If cavities do not close (or fill in), cultures will often become positive again even though chemotherapy is continued uninterruptedly; conversely, if cavities do close, cultures remain negative. 2. If cultures have not been rendered negative by the fourth month (a circumstance that is not known to the clinician until the sixth month because of the time-consuming nature of the test), there is little hope of their becoming negative solely by a continuation of chemotherapy. 3. Cultures that are still positive by the sixth month usually consist of bacilli that are resistant to streptomycin, though frequently they have retained their sensitivity to *p*-aminosalicylic acid. This is more likely to be true when a regimen of daily administration of streptomycin and *p*-aminosalicylic acid is employed, in contrast to 1 gm. of streptomycin twice weekly and daily *p*-aminosalicylic acid.

The target point is reached with the successful accomplishment of (1) stability of lesions (the maximum resolution of non-necrotic lesions present at the onset of chemotherapy and the formation of no new ones), (2) the closure of all cavities, and (3) the elimination of tubercle bacilli from the sputum. Clinical experience has shown that the termination of chemotherapy before the target point is reached is unwise, since relapse often follows. How much more chemotherapy is necessary after the target point has been reached is not known. The study on the optimum duration of chemotherapy will attempt to answer this question. Only the cases that reach the target point will be allocated at random for studies on duration of chemotherapy. One group will receive chemotherapy for three months after the target point has been reached, another for six months, and the third for nine months thereafter.

In the absence of precise knowledge regarding optimum duration of chemotherapy, it is believed at present that the minimum period of treatment should be 12 months, or 4 to 6 months after certain goals more or less comparable to the target point are reached. Throughout this long period it is

8. D'Esopo, N. D.: Prolonged Chemotherapy of Pulmonary Tuberculosis, Minutes of the Eighth Streptomycin Conference, Veterans Administration, Washington, D. C., Nov., 1949.

generally agreed that treatment should not be interrupted—there must be no short courses with "rest periods" in between, because resistant bacilli may make their appearance and such a situation cannot be reversed by a resumption of therapy with the same drugs.

Bacteriology of Closed Necrotic Lesions.—An inquiry into the viability of tubercle bacilli in necrotic lesions that are resected during the course of prolonged chemotherapy has been one of the most significant recent developments in the cooperative study.[2b] The question was raised as a result of certain bacteriological studies performed during prolonged therapy with streptomycin and *p*-aminosalicylic acid combined. In a number of these cases, residual lesions resected by the wedge technique were found to be either encapsulated necrotic foci or filled-in cavities. The necrotic lesions—and especially the filled-in cavities—contained myriads of tubercle bacilli visible on stained smears, but efforts to culture them were successful in only 10 to 15% of cases. These findings have now received wide confirmation.[2c]

It should be emphasized that these apparently nonviable bacilli are found in the "closed" necrotic lesions, best illustrated by the filled-in cavity. It is usually possible, on the contrary, to culture bacilli from air-containing cavities even after extensive chemotherapy.

The inability to cultivate viable bacilli from closed necrotic lesions or to produce tuberculous infection with them in susceptible laboratory animals has raised the question of their viability. In the opinion of some bacteriologists, no evidence for nonviability has been presented[2c]; the inability of organisms to reproduce, they say, does not necessarily mean that they are dead. They believe that the bacilli have been modified in some way by chemicals (such as fatty acids or spermine) in the closed lesion or by chemotherapy and may now require special techniques, still to be devised, in order to demonstrate their viability. Other bacteriologists are certain that these bacilli are dead.

The subject has stimulated a great deal of investigation in a rather old field.[9] Lesions have now been resected without having been subjected to chemotherapy, with essentially the same findings, provided, again, the lesions are closed.[2c] It is clear, therefore, that chemotherapy is not a prerequisite for this phenomenon. That bacilli die in closed necrotic lesions under natural conditions has long been known. The consistency with which nonviable bacilli are found in closed necrotic lesions during chemotherapy suggests—but only suggests—that chemotherapy is something more than an instrument in bringing about the "closed" state and that the drugs may have an active role in the death of bacilli—assuming that they are dead.

The possibility that bacilli may not survive in necrotic lesions has raised many practical problems in the use of chemotherapy, such as whether closed necrotic lesions should be resected if bacilli do die in them. The pathologist might state that these lesions are not healed and that morphologically they are potentially dangerous, since careful dissection often reveals debris-filled communicating bronchi that might easily serve as the pathway for a future relapse. In fact, such morphological features, especially the frequency of bronchial communications, were the rationale for resecting these lesions in the first place. Clinicians interpret these bacteriological data in various ways. Some are persuaded that the bacilli are dead; therefore they see no indication to resect such lesions simply because they are necrotic. Others are more impressed with the necrotic features of the lesions and, fearing that the bacilli merely appear dead, advocate resection. Still others are inclined to advise resection for the larger residual necrotic lesions but agree to allow small lesions to go unresected.

The best clinical application of these exciting bacteriological data is not known. At the Twelfth Conference, steps were taken toward designing controlled studies in order to learn how residual necrotic lesions should best be treated. Until such studies are completed, the decision to resect or not to resect will have to be made in a great many cases without precise knowledge of the natural fate of these lesions. These decisions should be a joint effort of physicians and surgeons, as such a team is in the best position to deal with factors of which the significance is now unknown. These factors are the number, size, and location of residual necrotic lesions and certain details of chemotherapy—the very factors, in short, that controlled studies are designed to clarify.

Chemotherapy and Surgery.—The relationships between chemotherapy and the surgery of pulmonary tuberculosis have undergone important changes since the introduction of prolonged combined regimens. The short courses of drug therapy (42 to 120 days) in use from 1946 to 1949 were principally of prophylactic value insofar as thoracic surgery was concerned. They were designed to help the patient through an acute phase of his disease or to prevent the complications of surgical procedures. In serving these ends, they were moderately successful. The timing of chemotherapy and surgery was of the greatest importance at that time, since bacterial resistance occurred quickly and much could be lost by delaying surgery too long. The prolonged combined regimens have increased the period of effective preoperative chemotherapy; thus, the timing of chemotherapy and surgery need not be planned as meticulously as formerly. This is especially true during the first six months of chemotherapy in previously untreated patients since relapses are few and the development of bacterial resistance is unusual during this period.

Prolonged chemotherapy has also given new indications for certain surgical procedures. Thus, chemotherapy may be used for long periods of time to heal the non-necrotic component of the disease, after which the residual necrotic lesions may be resected. This seems to be a reasonable approach. Some physicians, however, believe that portions of the lung that are heavily involved cannot be restored to functional integrity by chemotherapy and had best be resected. They contend that such lesions can be resected in the early weeks during a course of chemotherapy with very little risk, and at a great saving of time for the patient. Others believe that these portions of lung tissue are worth saving and that the resection of residual necrotic lesions after prolonged chemotherapy is the more conservative procedure. The point is yet to be settled.

The lessened importance of the timing between chemotherapy and surgery is not applicable to all cases. In patients whose cavities do not close during chemotherapy, the timing of the surgical procedure continues to be a matter of the greatest importance. It should be performed without further delay if experience suggests that the cavities will not close with further chemotherapy.

A large mass of statistical data bearing on chemotherapy and surgery was collected from 50 hospitals for the Twelfth Conference. The data showed that combined streptomycin and *p*-aminosalicylic acid therapy is better than streptomycin alone in affording protection against complications in thoracic surgery, that an original course of therapy is more effective than re-treatment, and that complications increase as the magnitude of the surgical procedure increases. (Complications are more numerous after lobectomy than after segmental resection and more numerous after pneumonectomy than after lobectomy.)

Since 1946, the use of chemotherapy with regard to surgery has gone through several phases and continues to change. Originally the emphasis was upon protection for thoracic surgery. Recently, the prolonged regimens have enabled more patients to become candidates for procedures such as lobectomy and segmental resection, very probably with a lower incidence of complications. Still more recently, surgery has been used to remove what chemotherapy cannot heal. The point has now been reached where the necessity for resecting closed necrotic lesions is open to question. It is quite possible that the time may be approaching when chemotherapy will be definitive therapy in many cases in which it was previously only a preparation for surgical procedures.

Chemotherapy in Tuberculous Meningitis and Miliary and Renal Tuberculosis.—In the early days of the cooperative study, the whole gamut of tuberculosis was studied, with a different protocol for every type of the disease from sinusitus

9. Sweany, H. C.: Age Morphology of Primary Tubercles, Springfield, Ill., Charles C Thomas, Publisher, 1941. Sweany, H. C.: Age Characteristics of Tubercles, Am. Rev. Tuberc. **46**: 329 (Sept.) 1942. Sweany, H. C.; Levinson, S. A., and Stadnichenko, A. M. S.: Tuberculous Infection in People Dying of Causes Other Than Tuberculosis, ibid. **48**: 131 (Sept.) 1943. Canetti, G.: Le bacille de Koch dans la lésion tuberculeuse du Poumon, France, Editions Médicales Flammarion, 1946.

to pericarditis. A good deal of useful data were gathered. Most of these studies have been discontinued, partly because the knowledge that was sought has been gained, but chiefly because the drug regimen that is superior in one situation is equally superior in the other. Pulmonary tuberculosis was chosen for investigation because of its frequency, although meningitis has special investigative advantages, and superficial lesions of the mucous or serous membranes respond more readily to chemotherapy than do parenchymatous lesions. For example, tuberculous laryngitis, formerly an agonizing experience for both patient and physician, may even be healed by amithiozone, which is regarded as a third-class drug for pulmonary tuberculosis. By and large, the virtues and frailties of the regimens that have been discussed in this report are as applicable to extrapulmonary as they are to the pulmonary tuberculosis. In two instances, however, meningeal and genitourinary tuberculosis, a continuing study of extrapulmonary tuberculosis has seemed desirable.

Tuberculous meningitis (and with it, for purposes of present convenience, acute disseminated miliary tuberculosis) is, in theory, the ideal testing ground for an antituberculosis drug because, prior to chemotherapy, it had a mortality rate of 100%. If even a single patient survived therapy, it became certain that the drug used was an effective antituberculosis agent.

Between April, 1946, and May, 1947, 100 patients with meningeal or miliary tuberculosis, either alone or in combination, were treated with streptomycin alone in Veterans Administration Hospitals. A five year follow-up on this series is now available. Five of 47 patients (11%) with meningitis are alive (with 7% "entirely well"). Nine of 19 patients (47%) with miliary tuberculosis are alive (with 37% "entirely well"). The results in this first series were spectacular at the time (37% of the meningitis patients were alive 4 to 14 months after the initiation of therapy), but they were not nearly as spectacular as subsequent reports, particularly those from Europe. The details of chemotherapy varied in the different series (in one series, thiazolsulfone was added), but the most obvious difference was that our case material consisted entirely of adults whereas the others consisted almost entirely of children. That difference may or may not contain the explanation.

Since the 1946-1947 series, the survival rates have gradually improved in these groups of patients in our cooperative study, but a striking and definite change occurred only when *p*-aminosalicylic acid was used in combination with streptomycin (or dihydrostreptomycin). In view of the low regard in which members of the conferences hold the therapeutic efficacy of *p*-aminosalicylic acid, this consequence was surprising. In the 600 odd cases reported to the Twelfth Conference, the three year survival rate in tuberculous meningitis among patients receiving this combined therapy had risen to approximately 50% and, in miliary tuberculosis, to approximately 80%.[2c] The addition of isoniazid to the armamentarium may be of further assistance. It has already been shown to be effective in the treatment of meningitis and, although the small series of cases (13) reported upon did nothing more than strengthen that belief, it was urged that it be incorporated with its two predecessors in the treatment of future cases. Because of the imminent hazard of meningitis, the members of the conferences have not felt justified in recommending that cases be allocated at random for different regimens. The members of the conferences have long and strongly supported the desirability of administering streptomycin by both intrathecal and intramuscular routes and are now well convinced that the former technique is unnecessary. There is firm agreement, which seems unlikely to change, that chemotherapy should be continued for at least 12 months. The intrathecal or intraventricular injection of tuberculin has not been attempted by the cooperating hospitals.

The results of chemotherapy in 545 cases of genitourinary tuberculosis treated in the seven years since 1946 were also reported to the Twelfth Conference. The descriptions of many of the earlier cases were incomplete, and random allocation had been inadequate or not attempted. Nevertheless, accepting the conversion of urine from positive to negative as the criterion of effective therapy, certain general conclusions can be drawn that are remarkably analagous to those described in meningitis. Patients receiving courses of streptomycin alone for the relatively short period of four months showed a conversion rate of less than 20% in the presence of medium or large-size renal lesions at the time of a five year follow-up examination. When *p*-aminosalicylic acid was added to streptomycin, and to a still greater extent when the duration of treatment was extended to 12 months, the conversion rate increased to 80% in the presence of similar lesions two years after the beginning of therapy. Whether this impressive figure will be maintained during more prolonged periods of observation remains to be seen. Preliminary evidence of the effectiveness of isoniazid is encouraging, and there is little or no indication of renal toxicity. A combination of streptomycin and isoniazid was agreed upon as the regimen of choice for the calendar year 1953. Nephrectomy (or, under certain circumstances, partial resection), in addition to chemotherapy, is still regarded as the procedure of choice in the presence of extensive unilateral renal involvement.

Other Projected Studies.—Two subjects proposed at the Twelfth Conference as appropriate for future investigation, a controlled study of residual necrotic lesions and the duration of chemotherapy, have already been touched upon. Other studies to be undertaken are concerned with the value of pneumoperitoneum in the treatment of patients receiving prolonged chemotherapy and the need for rest during chemotherapy.

The study concerned with pneumoperitoneum is an inquiry into the possible advantages of adding this form of collapse in the treatment of cavitary disease. When chemotherapy consisted of short courses of 42 to 120 days, the value of collapse therapy could scarcely be questioned. Indeed chemotherapy and collapse therapy seemed to supplement each other; the former was directed toward the healing of nonnecrotic lesions and the latter toward the closure of cavities. Prolonged chemotherapy, however, frequently brings about the closure of cavities without the aid of collapse measures. What, then, are the present indications for pneumoperitoneum? Is the size of the cavity a determining factor in the decision? Will cavities close more rapidly if treated with both types of therapy simultaneously? These are some of the questions the study seeks to answer.

The projected study of rest represents a wide departure from the traditional attitude towards this best-established mode of tuberculosis therapy. The impetus of this study is the success of the prolonged chemotherapy regimens and the hope that they will, by themselves, prove to be definitive. Patients in this study are to be highly selected. Patients with advanced disease and those who have previously received any form of chemotherapy for tuberculosis are to be excluded. One group in the study will receive prolonged chemotherapy along with the amount of rest customary in the hospital concerned; a second group, in other hospitals, will receive prolonged chemotherapy along with as much rest as is indicated by each patient's symptomatology.

The studies of rest, resection, and pneumoperitoneum that have been outlined are a search for the indications for definitive chemotherapy. If this goal appears strange, it is probably because it has been said too often that tuberculosis cannot be cured by drugs alone, that rest is indispensable for the treatment of tuberculosis under any circumstances, that cavitary disease requires some kind of collapse-therapy, or that tuberculosis cannot be considered healed as long as necrotic lesions persist. These generalities are undoubtedly valid for a great many cases of tuberculosis; for some, however, they seem to be no longer true. We must learn to identify these cases.

SUMMARY

The present report reviews the position of the major chemotherapeutic agents now used in the treatment of tuberculosis, especially the relative merits of streptomycin, *p*-aminosalicylic acid, and isoniazid. It includes, also, a few brief remarks on several lesser drugs, such as viomycin, oxytetracycline (Terramycin), and pyrazinamide (Aldinamide). About half of the report deals with the use of antituberculosis agents in a general sense. It discusses problems relating to the optimum duration of chemotherapy together with the protocol designed

by the Twelfth Conference on the Chemotherapy of Tuberculosis to study this point. The report also reviews the recent data concerning the viability of tubercle bacilli in closed necrotic lesions and discusses the significance of this fact in clinical practice. There is a brief section on the integration of chemotherapy and surgery. Two extrapulmonary tuberculous lesions, tuberculous meningitis and miliary renal tuberculosis, are briefly reviewed in the light of data submitted to the Twelfth Conference. Finally, two projected studies dealing with the integration of pneumoperitoneum in chemotherapy and of bed rest and chemotherapy are briefly mentioned.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

APPARATUS ACCEPTED

The following additional products have been accepted as conforming to the rules of the Council on Physical Medicine and Rehabilitation of the American Medical Association for inclusion in Apparatus Accepted. A copy of the rules on which the Council bases its action will be sent on application.

RALPH E. DE FOREST, M.D., *Secretary.*

Resp-Aid Iceless Oxygen Tent, Model 200

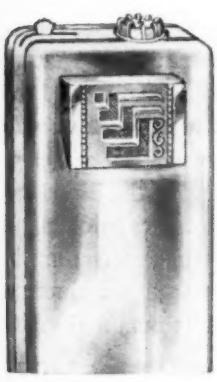
Respiration Aids, Inc., 424 E. 123rd St., New York 35.

The Resp-Aid Iceless Oxygen Tent is an apparatus for administering oxygen, which has been electrically temperature-conditioned, to a patient in bed. The apparatus includes a transparent canopy that covers the patient, and a cabinet that contains the machinery. It can be wheeled to the bedside on casters. The motor requires 60 cycle alternating current at 115 volts and draws 700 watts.

Resp-Aid Iceless Oxygen Tent, Model 200

Crated for shipment, the apparatus measures 103 by 60 by 70 cm. (40½ by 23½ by 26½ in.) and weighs 123 kg. (270 lb.). Unpacked, the cabinet containing the motor measures 159 (height including superstructure) by 41 by 59 cm. (53 by 16 by 23 in.) and weighs 87 kg. (190 lb.).

Evidence from sources acceptable to the Council showed that this apparatus was well made and gave good service.



Telex Hearing Aid, Model 952

Telex Hearing Aid, Model 952

Telex, Inc., Telex Park, St. Paul 1.

The Telex Hearing Aid, Model 952, is also called Super-Telex. It contains five vacuum tubes and requires two A-batteries (1.5 volt mercury cells) and one B-battery (45 volts). The body of the instrument measures 115 by 55 by 20 mm. and weighs 151 gm. In addition, the three batteries weigh a total of 100 gm., the receiver cord 3 gm., and the receiver 8 gm.

Evidence of satisfactory construction and performance, both for air and bone conduction, was obtained from sources acceptable to the Council.

S. & L. Enuresis Alarm, Model D

S. & L. Signal Company, 525 Holly Ave., Madison 5, Wis.

The S. & L. Enuresis Alarm is an electric device that sounds an electric bell when the bed pad is wet by a patient. It consists essentially of two parts: (1) a control box containing a 22.5 and a 6 volt battery and a bell and (2) a bed pad consisting of two rectangular bronze wire screens separated by a layer of cloth. These two parts are connected to the control box by a cable. The bronze screens measure 56 by 61 cm. (22 by 24 in.), and when the cloth between them is wet by a conducting fluid a sufficient current flows to set off the alarm. The alarm rings until it is switched off by the user.

S. & L. Enuresis Alarm, Model D

Packed for shipment the entire unit measures 20.3 by 61 by 33 cm. (8 by 24 by 13 in.) and weighs 5.9 kg. (13 lb.).

The Council obtained evidence that this device was helpful when used under medical supervision in cases of enuresis not attributable to physical disease.

Otarion Hearing Aid, Model C-15

Otarion Hearing Aid, Model C-15

Otarion, Inc., 4757 N. Ravenswood Ave., Chicago 40.

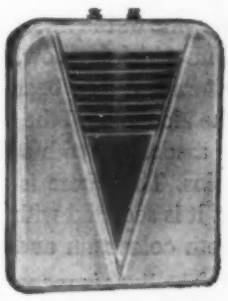
The Otarion Hearing Aid, Model C-15, incorporates one transistor with two vacuum tubes. It requires one mercury type 1.5 volt A-battery and one 15 volt B-battery. The body of the instrument measures 63 by 45 by 23 mm. and weighs 70 gm. The receiver, receiver cord, and two batteries bring the total weight to 108 gm.

Acousticon Hearing Aid, Model A-17

Dictograph Products Inc., 95-25 149th St., Jamaica 35, Long Island, N. Y.

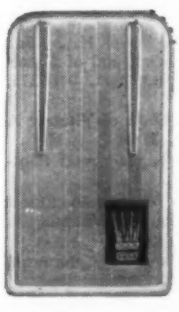
The Acousticon Hearing Aid, Model A-17, incorporates three vacuum tubes and requires one 1.5 volt A-battery and one 15 volt B-battery. It can be used with any one of 10 air earphones and 3 bone receivers, adjusted for different acoustic responses.

The body of the instrument, disregarding minor projections, measures 82 by 65 by 22 cm. and weighs 76.5 gm. With clip attachment, receiver, receiver cord, and batteries, it weighs 132.5 gm.



Acousticon Hearing Aid, Model A-17

Acousticon Hearing Aid, Model A-185



Acousticon Hearing Aid, Model A-185

Dictograph Products Inc., 95-25 149th St., Jamaica 35, Long Island, N. Y.

The Acousticon Hearing Aid, Model A-185, incorporates three vacuum tubes and requires one 1.3 volt A-battery and one 30 volt B-battery. It can be used with any one of 10 air earphones and 3 bone receivers, adjusted for different acoustic responses.

The body of the instrument, disregarding minor projections, measures 77 by 45 by 22 mm. and weighs 73 gm. With receiver, receiver cord, and batteries, the total weight is 125 gm.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
535 N. DEARBORN ST. . . . . CHICAGO 10, ILL.
Editor . . . . . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
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Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

VITAMIN A IN LIVER CELLS

Although the indispensability of vitamin A in the diet has long been accepted, the precise mode of its action in the organism still remains to be demonstrated. To be sure, distortion of normal histogenesis and widespread metaplasia are recognized as more or less characteristic sequelae of the deficiency of this food factor; yet detailed information with respect to its influence on the chemistry of cellular processes is not available. There are, however, facts about vitamin A that will ultimately contribute to a better understanding of the mechanism of its action.

Inasmuch as the vitamin has the chemical structure of an alcohol, its existence in liver oil partially as an ester [1] might be expected; in one study [2] after experimental animals had been fed a concentrate of fish liver oil containing almost all the vitamin in the ester form, the vitamin A was largely present in the intestinal mucosa in the alcohol form, indicating that the original ester form had been hydrolyzed by the fat-splitting enzyme of the intestine much as is any food fat. Studies [3] with chicken, cow, and pig blood indicate that once vitamin A has been absorbed into the circulation both the alcohol and the ester forms are present but that each is associated with a different fraction of the plasma proteins. That there is a change in the form of vitamin A as it is secreted with milk fat is shown by the fact that in both colostrum and milk the ester form predominates.[4]

The liver is recognized as the main storehouse of vitamin A in the body. It was early shown that, in animals fatally poisoned with phosphorus, there was little if any diminution of vitamin A in the damaged liver, which suggests that the Kupfer cells may take over the vitamin-storing function of the hepatic cells.[5] A similar reciprocal function of these two kinds of liver cells was observed during hypervitaminosis in studies in which the fluorescent microscope was used.[6]

Recently, a closer approach to the localization of vitamin A in the cell was made through the fractional centrifugation of liver cell homogenates; by this device a soluble portion is separated from the cell solids and then the latter are further fractionated into the nuclear part, the mitochondria and the microsomes. In one such experiment,[7] vitamin A (undifferentiated) was found largely in the soluble part, with the mitochondrial fraction of the solids containing most of the remainder. More recently, with similar techniques but with the vitamin A partitioned into ester and alcohol fractions, it was found [8] that the ester form is preponderate in the hepatic cell and that this is largely in the "cream" layer of the nonsolids fraction. Of the alcohol form, about two-thirds is in the "cream" layer and the rest divided between the remaining supernatant and the microsomes. The difference in distribution of the ester and the alcohol form of the vitamin may be due to the demonstrated association of each with different proteins within the cell.

The available data on the distribution of vitamin A within the tissue cells are somewhat conflicting in detail, owing largely to the imperfections of the chemical and cytological techniques involved. It may be expected, however, that in the future such studies will be extended, with more technical skill, to other nutrients and therapeutic agents and to other tissue cell types, with a consequent better understanding of many disease processes.

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4. Parrish, D. B.; Wise, G. H., and Hughes, J. S.: State of Vitamin A in Colostrum and in Milk, J. Biol. Chem. **167**: 673, 1947.

5. Lasch, F.: Vitamin A Metabolism and Liver in Experimental Phosphorus Poisoning, Klin. Wchnschr. **14**: 1070, 1935.

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7. Collins, F. D.: Distribution of Vitamin A in Rat-Liver Cytoplasm, Proceedings of the Biochemical Society, Biochem. J. **51**: xxxviii, 1952.

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ACQUIRED AFIBRINOGENEMIA IN PREGNANCY

Severe uncontrollable hemorrhage associated with nonclotting of the blood is a dreaded complication of certain obstetric conditions, particularly premature separation of the normally implanted placenta. Attention was first drawn to this condition in 1901 by DeLee, who described it as a temporary hemophilia. Since then, various investigators have sought to determine the nature of the coagulation defect. In 1915, Williams likened the hemorrhagic lesions in abruptio placentae to those seen after poisoning by certain varieties of snakes and suggested that a toxic substance circulating in the blood led to changes in the vessels that permitted escape of blood into the tissues. Willson in 1922 suggested that in abruptio placentae there was liberation from the placenta of a hemorrhagic toxin that exerted its maximal effect locally in the form of retroplacental bleeding and thus led to the placental separation. He further suggested that, when this toxin was absorbed into the maternal circula-

tion, general toxemia and, on occasion, severe hemorrhage would result.

A fresh approach was provided by Dieckmann, who, in 1936, found that the blood fibrinogen levels were greatly reduced in patients who hemorrhaged after abruptio placentae.[1] Dieckmann's observations have been amply confirmed by subsequent investigators,[2] and various hypotheses have been advanced to explain this reduction of blood fibrinogen despite adequate hepatic function. Dieckmann thought that the reduction was due to the mobilization of fibrin at the site of the placental separation. Moloney, Egan, and Gorman, on the other hand, attributed the afibrinogenemia to the presence of a fibrinolysin.[2a] Other investigators, such as Schneider,[3] Page and his associates,[2d] and Reid and co-workers,[4] have presented what in the light of present knowledge is probably the most plausible explanation. These investigators point out that thromboplastin or a thromboplastin-like material has been shown to exist in placental tissue and in amniotic fluid. They postulate that under certain conditions enough of this thromboplastic substance may be forced into the maternal circulation to bring about a conversion of the fibrinogen to fibrin, which in turn is deposited on the walls of the blood vessels as fibrin thrombi. This concept gains support from reports that injection of placenta extracts or of thromboplastin into animals [illegible] defibrination of the blood, as well as increasing time and extensive vascular fibrin deposits. It has been suggested that in abruptio placentae the increased intrauterine pressure occasioned by the retroplacental clot favors the entrance of amniotic fluid into the maternal circulation. This would explain why hemorrhagic difficulties are not seen when the retroplacental clot is small, why the process of defibrination is arrested after artificial rupture of the membranes, and why afibrinogenemia is not seen in placenta previa, when the blood can escape freely through the cervical os.

While most attention has been focused on the coagulation defect occurring in abruptio placentae, there is evidence to indicate a similar sequence of events in certain other conditions, particularly in long-standing intrauterine fetal death[5] and in the so-called syndrome of amniotic fluid embolism.[6] In the former, Reid and his associates suggest that placental autolysis results in a high concentration of thromboplastic material, which may enter the maternal circulation under the impetus of uterine contractions. In the later instance, they suggest entry of amniotic fluid with its defibrinating material is favored by tumultous contractions such as may follow the administration of posterior pituitary preparations. These investigators believe that the severe manifestations of this condition may be related to intravascular clotting and to uncontrollable bleeding subsequent to defibrination rather than to embolic effects of the particulate matter of the amniotic fluid infusions and an associated anaphylactoid reaction, as postulated by Steiner and Lushbaugh.[7]

Recognition of the presence of acquired afibrinogenemia permits a rational approach to the therapy of uncontrollable bleeding in pregnancy, and numerous investigators have attested to the value of fibrinogen or of massive whole blood transfusions in restoring the clotting mechanism.[8] In the severer cases of abruptio placentae Reid considers that restoration of the clotting ability of the blood should precede any surgical attempt at delivery other than rupture of the membranes. In the syndrome of amniotic fluid embolism, restoration of the blood fibrinogen offers a therapeutic approach to a condition previously considered hopeless. In cases of long-standing fetal death, it is suggested that periodic studies of the blood be undertaken so that, if alterations in the clotting mechanism are encountered, prompt hospitalization and suitable treatment may be instituted without delay.

ACCIDENTS IN CHILDREN

A notable decrease in infant mortality and in the death rate from childhood diseases has been brought about by the nation's physicians during the last half century. However, despite the efforts put forth by the medical profession to protect the country's future citizens, childhood mortality continues high because of accidents—accidents that, for the most part, are preventable. The accident death rate among children is being reduced only about one-third as fast as the rate for death by disease. Preventable accidents are the leading cause of death in the age group of 1 to 14 years, killing more children than the combined mortality of the next six causes of death—

1. Dieckmann, W. J.: Blood Chemistry and Renal Function in Abruptio Placentae, Am. J. Obst. & Gynec. **31**: 734, 1936.

2. (*a*) Moloney, W. C.; Egan, W. J., and Gorman, A. J.: Acquired Afibrinogenemia in Pregnancy, New England J. Med. **240**: 596, 1949. (*b*) Weiner, A. E.; Reid, D. E., and Roby, C. C.: Coagulation Defects Associated with Premature Separation of the Normally Implanted Placenta, Am. J. Obst. & Gynec. **60**: 379, 1950. (*c*) Schneider, C. L.: Fibrin Embolism (Disseminated Intravascular Coagulation) with Defibrination as One of the End Results During Placenta Abruptio, Surg. Gynec. & Obst. **92**: 27, 1951. (*d*) Page, E. W.; Fulton, L. D., and Glendening, M. P.: The Cause of the Blood Coagulation Defect Following Abruptio Placentae, Am. J. Obst. & Gynec. **61**: 1116, 1951.

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4. Weiner, A. E.; Reid, D. E., and Roby, C. C.: Incoagulable Blood in Severe Premature Separation of the Placenta: A Method of Management, Am. J. Obst. & Gynec. **66**: 475, 1953.

5. Reid, D. E.; Weiner, A. E.; Roby, C. C., and Diamond, L. K.: Maternal Afibrinogenemia Associated with Long-Standing Intrauterine Fetal Death, Am. J. Obst. & Gynec. **66**: 500, 1953.

6. Ratnoff, O. D., and Vosburgh, G. J.: Observations on the Clotting Defect in Amniotic-Fluid Embolism, New England J. Med. **247**: 970, 1952. Reid, D. E.; Weiner, A. E., and Roby, C. C.: I. Intravascular Clotting and Afibrinogenemia: The Presumptive Lethal Factors in the Syndrome of Aminotic Fluid Embolism, Am. J. Obst. & Gynec. **66**: 465, 1953.

7. Steiner, P. E., and Lushbaugh, C. C.: Maternal Pulmonary Embolism by Amniotic Fluid, J. A. M. A. **117**: 1245 (Oct. 11) 1941.

8. Footnotes 2, 5, and 6. Ranney, B.: Abruptio Placenta, Blood Defibrination, Lower Nephron Syndrome, and Sequellae: A Case Report, South Dakota J. of Med. **6**: 6, 1953. Goodfriend, M. J.; Shey, I. A., and Siegelbaum, H. L.: Defective Blood Coagulation Associated with Premature Separation of the Placenta, Am. J. Obst. & Gynec. **65**: 1034, 1953.

pneumonia, congenital defects, cancer, tuberculosis, leukemia, and heart disease—and killing many, many more children than poliomyelitis.

According to a recent report of the Children's Bureau of the Department of Health, Education, and Welfare, the 1949 accident death rate of children under one year of age was 72.1 per 100,000. Home accidents of various kinds accounted for infant deaths at the rate of 43 per 100,000. The largest single cause of accidental death in infancy was the inhalation or ingestion of objects; fire, explosions, and burns and motor vehicle accidents followed in that order. Children 1 to 4 years of age died from accidents at the rate of 37.8 per 100,000, with motor vehicle accidents; fires, explosions, and burns; and drownings as the leading causes.

"Accident Facts, 1953," published by the National Safety Council, points out that in 1952 accidental deaths among children 5 to 14 years of age totaled 6,100. Of these deaths, 2,450 were classed as due to motor vehicles, 1,150 occurred in the home, 2,300 were classed as public non-motor-vehicle accidents, and 200 were classed as occupational. In addition, thousands of school-age children are injured sufficiently each year to require the attention of a doctor or to cause absence from school of one-half day or more. Injuries occurring in school buildings account for 26% of such cases, on school grounds for 29%, going to and from school for 5%, at home for 17%, and in other places, chiefly public, for 23%. In school buildings, about one-third of the injuries occur in gymnasiums; classrooms are next, with vocational shops, stairways, and corridors following. On school grounds, injuries occur somewhat more frequently during organized activities than during unorganized ones. In organized activities they happen most frequently in football and baseball; in unorganized activities, they occur most frequently in falls and running accidents. Going to and from school, the principal source of injury is motor-vehicle accidents.

Although there is little a physician can do directly to prevent childhood deaths and disabilities due to accidents, there is much he can do indirectly. To most persons a physician is more than a doctor of medicine—he is a friend. As such a friend, a physician can proffer advice. It is up to the physician to take the initiative to instruct parents and school personnel, specifically, and the entire community, generally, in childhood safety problems. Adults must be made to understand the accident problem of children and must be made as concerned about it as they are about childhood diseases. As children do not always conform to the practices that would insure their greatest safety, the cooperation of adults is necessary. Only by such cooperation can the toll of childhood death and disability due to preventable accidents be cut. Children deserve the chance to grow up—it is up to every adult to give them that chance.

TREATMENT OF PULMONARY EDEMA

Inhalation of a vapor obtained by oxygen bubbling through 50% ethyl alcohol-water solution is being used for the treatment of pulmonary edema that has resisted all other forms of therapy. In pulmonary edema there is a transudation of blood elements through altered alveolar capillary walls into the alveoli, and this fluid is churned into a froth by the respiratory activity. The proponents of alcohol vapor inhalation in the treatment of pulmonary edema believe that there is an alteration of the surface tension in the alveoli producing a collapse of the foam bubbles and that the alcohol vapor penetrates into the finer air spaces.

The oxygen is delivered from a cylinder through a simple vaporizer consisting of a 250 cc. bottle half filled with 50% ethyl alcohol-water solution, with a rubber stopper holding two large-bore metal tubes. One tube reaches to the bottom of the bottle and delivers the oxygen, which bubbles through the solution; the other tube is above the fluid level and carries the alcohol-laden oxygen to the meter mask. Sprayers and filters are not used in this set-up, so that pressure will be kept at a maximum.

This apparatus should never be used when there is an open flame in the same room. A 50% alcohol solution in water will burn easily when ignited with an open flame. The bluish flame of the alcohol dies out when the alcohol content reaches 20% or less. A 25% solution can be ignited in the presence of oxygen but not in air. A 30% solution will ignite in the presence of air or oxygen. Because a 50% alcohol-water solution, at room temperature, requires a spark of about 20,000 electrostatic volts at the surface to ignite it, there is practically no danger of static ignition. Care must be taken, however, to prevent ignition by open flame or by "flash-flame," which may be produced by the surging of oxygen through the regulator under too great a pressure, and carrying it through the alcohol-water mixture.

TETANUS IMMUNIZATION FOR HORSEMEN

Adults who ride horses all year round and who are frequently in stables should be protected against tetanus by the use of tetanus toxoid followed by booster injections. Ordinarily, two doses of 0.5 cc. of depot antigen or three doses of 0.5 cc. of fluid antigen constitute a reliable routine for basal immunization. Subsequent booster doses, conveniently given at intervals of one to two years or at the time of an injury, may be given in amounts of 0.1 cc. of either depot or fluid antigen, given deep subcutaneously. Some favor the intracutaneous route (fluid toxoid). It is significant that booster injections are effective for as long as 10 years after basal immunization. Moreover, if there is delay in prophylaxis with tetanus toxoid booster injection, severe injury, marked physical debility or blood loss, or equivocal history concerning injections of toxoid, tetanus antitoxin (not less than 10,000 units) is needed in addition to booster injections.

ORGANIZATION SECTION

ABSTRACT OF PROCEEDINGS OF THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION AT THE CLINICAL MEETING IN ST. LOUIS, DEC. 1-4, 1953

(Continued from page 1555)

No. 18. Resolutions on Joint Commission on Accreditation of Hospitals

Dr. Cleon A. Nafe, Indiana, introduced the following resolutions, which were referred to the Reference Committee on Miscellaneous Business:

WHEREAS, Considerable misunderstanding exists among physicians concerning the rules and regulations of the Joint Commission on Accreditation of Hospitals concerning the role of the Department of General Practice in a hospital; and

WHEREAS, It is not clear what methods of appeal are available to a hospital and its staff when the findings of the Commission are considered unjust; therefore be it

Resolved, That this House of Delegates of the American Medical Association request the Joint Commission on Accreditation of Hospitals to publish an article, or series of articles, in THE JOURNAL of the American Medical Association and other official publications circulating among the medical and hospital professions, to acquaint the medical-hospital profession with the regulations, bylaws, and their interpretations; and be it further

Resolved, That the commission clarify the methods by which an aggrieved hospital or its staff may appeal a decision with which they are not in agreement.

Report of Reference Committee on Miscellaneous Business

Dr. H. Gordon MacLean, Chairman, presented the following report, which was adopted:

Res. No. 18 on Joint Commission on Accreditation of Hospitals: Your committee approves this resolution and recommends that this House of Delegates of the American Medical Association request the Joint Commission on Accreditation of Hospitals to publish an article or a series of articles in THE JOURNAL of the American Medical Association and other official publications circulating among the medical and hospital professions, to acquaint the medical-hospital professions with the regulations, bylaws, and their interpretations, and that the commission clarify the methods by which an aggrieved hospital or its staff may appeal a decision with which they are not in agreement.

No. 19. Resolutions on Proposed Amendment to Bylaws Re Powers of Judicial Council

Dr. George A. Unfug, Colorado, introduced the following resolutions, which were referred to the Reference Committee on Amendments to the Constitution and Bylaws:

WHEREAS, The Judicial Council frequently has presented to it for decision controversies between contending parties or is asked for and gives its opinion on matters with respect to which there are differences of view; and

WHEREAS, The full hearing of both parties to a controversy is essential to a just determination of it and full cognizance of all views is essential to the expression of sound opinion and it is desirable that there should be equal opportunity for all interested persons to be heard; and

WHEREAS, Interpretation of ethical principles of general application ought to be subject to examination by the House of Delegates; therefore be it

Resolved, That Division Three, Chapter XI, Section 10 (A) (1) of the Bylaws of the Association be and hereby is amended to read as follows:

(1) The judicial power of the Association shall be vested in the Judicial Council whose decision shall be final unless rejected or modified by the House of Delegates. All decisions and opinions of the Judicial Council shall be reduced to writing and kept on file at the Association headquarters. All decisions and opinions of the Judicial Council shall be open to inspection by any member of the Association at the headquarters of the Association. Any such opinion may be brought before the House of Delegates by any delegate at any of the three regular meetings of the House next succeeding the rendition of the opinion. The House may affirm or modify such opinion or return the matter to the Judicial Council for re-examination; and be it further

Resolved, That Division Three, Chapter XI, Section 10 (A) of the Bylaws of the Association be and hereby is amended by adding at the end thereof a new paragraph as follows:

(7) In matters with respect to which an investigating jury is not requested, the Judicial Council shall observe the following procedure:

(*a*) No issue between parties shall be decided by the Judicial Council without affording to each party the opportunity to be heard in the presence of each other either personally or by a representative of his choice both orally and in writing. All parties shall be notified of the time and place of hearing in ample time to make the right to be heard effective.

(*b*) No opinion (except decision of specific controversies under paragraph (*a*) above) shall be rendered by the Judicial Council until at least 60 days after the request for opinion (or the tentative opinion if no request has been made) shall have been published in THE JOURNAL of the American Medical Association for at least two consecutive issues. Any member of the American Medical Association or a designated representative may present his views on such matter to the Judicial Council in writing and, if any constituent or component society so requests, hearing shall be held by the Judicial Council at which any recognized medical society which desires it shall be heard by a representative of its choice.

Report of Reference Committee on Amendments to the Constitution and Bylaws

Dr. William L. Benedict, Chairman, submitted the following report, which, on motion duly seconded and carried, was referred to the Council on Constitution and Bylaws with the request that it report to the House at the San Francisco Session in June, 1954:

Your committee has considered Resolution No. 19 proposing an amendment to Division Three, Chapter XI, Section 10-A of the Bylaws of the Association relating to the interpretation of ethical principles. The committee believes that decisions of the Judicial Council should not be reviewed by a legislative body, namely the House of Delegates. All decisions and opinions of the Judicial Council are open to inspection by any member of the Association at the Association headquarters; therefore, the committee recommends that the proposed amendment be not approved.

The proposed amendment 7(*a*) will add no safeguards not already employed by the Judicial Council and the committee is convinced that the rights of members and of component and constituent societies are adequately protected; therefore, the committee recommends that the proposed amendment be not approved.

It is the opinion of your committee that it would be unwise and indiscreet to publish in THE JOURNAL of the American Medical Association all decisions of the Judicial Council; therefore, the committee disapproves of the proposed amendment 7(*b*).

No. 20. Resolution on Joint Committee on Hospital-Patient Relationship

Dr. Herbert B. Wright, Ohio, introduced the following resolution, which was referred to the Reference Committee on Miscellaneous Business:

WHEREAS, In June, 1953, the House of Delegates of the American Medical Association approved "A Report of the Joint Committee on Hospital-Physician Relationships of the Board of Trustees of the American Medical Association and the American Hospital Association" and in so doing stated that the general principles contained in the joint report were in some respects more specifically stated in the "Guides for Conduct of Physicians in Relationships with Institutions" which had been finally adopted by the House of Delegates in Los Angeles in December, 1951; and

WHEREAS, Despite the statement referred to in the preceding paragraph, it has been claimed that the action in 1953 in some way superseded or modified the "Guides" adopted in December, 1951; and

WHEREAS, The sale of the professional services of a physician by a hospital, corporation, or other lay person involves the splitting of professional fees and the practice of medicine by a layman and is thus a violation of the Principles of Medical Ethics irrespective of whether exploitation exists; and

WHEREAS, It is the duty of the House of Delegates of the American Medical Association clearly and unequivocally to state the ethical principles which should guide a physician although the specific application of them and the enforcement of them is a local matter which may vary slightly in accordance with local conditions; now therefore be it

Resolved, That the House of Delegates of the American Medical Association reaffirms and readopts the "Guides for Conduct of Physicians in Relationships with Institutions" as adopted by the House of Delegates at Los Angeles in December, 1951.

No. 21. Resolutions on Employment of Physicians by Hospitals

Dr. Wesley W. Hall, Nevada, introduced the following resolutions, which were referred to the Reference Committee on Miscellaneous Business:

WHEREAS, Under date of June 22, 1953, the Judicial Council gave an opinion on the question of whether a doctor employed on a salary by a hospital is guilty of unethical practice; and

WHEREAS, The position of the American Medical Association on this point should be clear and unequivocal; therefore be it

Resolved, That a doctor employed on a salary basis by a hospital is not guilty of unethical practice unless, under the terms of his employment, the hospital may sell for its own account the doctor's professional services; and be it further

Resolved, That the amount of any payment from a hospital or other lay agency to a physician is material only insofar as it is indicative of the relationship between the physician and such agency. If the hospital collects fees for the physician's professional services, then employment of the physician on salary is conclusive evidence that the hospital is selling the physician's professional services; and be it further

Resolved, That it is unethical for a physician to permit a hospital or any other lay agency or person to sell his professional services to patients for compensation to such agency. In such case, the ethical nature of such relationship is not affected by the manner in which the physician is paid or if he is paid at all. Such relationship is contrary to the interests of the patient in that it tends (*a*) to prevent the free choice of physician, (*b*) to interpose a third party between the physician and his patient (*c*) to permit lay practice of medicine, (*d*) to encourage fee splitting, and (*e*) to commercialize the practice of medicine. This does not refer to payments by physicians of insuring agencies on the account of the patient from funds paid by the patient as premiums. If no charge is made for the physician's services or his work does not constitute the practice of medicine, then no ethical question arises; and be it further

Resolved, That the forgoing ethical principles should be followed by all physicians as previously declared by this House in the "Guides for Conduct of Physicians in Relationships with Institutions" which is hereby expressly reaffirmed; and be it further

Resolved, That if a physician or other lay agency grants to a hospital the power of disposition over his professional services by becoming, for example, a salaried employee of a hospital, under circumstances that permit the hospital to sell those services for its own account, then such circumstances "permit exploitation" as that phrase is used in "A Report of the Joint Committee on Hospital-Physician Relationships" approved by this House in June, 1953.

No. 26. Resolutions on Hospitals Practicing Medicine

Dr. Thurman B. Givan, New York, introduced the following resolutions, which were referred to the Reference Committee on Miscellaneous Business:

WHEREAS, The Medical Society of the State of New York has expressed its disapproval of hospitals engaging in the practice of medicine; and

WHEREAS, Plans are being introduced by administrative decision, often without prior consultation of the medical profession to finance hospitals and medical college deficits by requiring practicing physicians to contribute their earnings above a limit solely determined by the hospital; therefore be it

Resolved, That the American Medical Association disapproves of hospitals engaging in the practice of medicine; and be it further

Resolved, That participation of a hospital in the professional earnings of a physician (except for equitable payment to the hospital for services it renders the physician, such as provision of office space, secretarial service, and supplies) constitutes practice of medicine by the hospital and is therefore disapproved.

Report of Reference Committee on Miscellaneous Business

Dr. H. Gordon MacLean, Chairman, presented the following report, which was adopted:

Res. No. 20 on Joint Commission on Hospital-Physician Relationships; Res. No. 21 on Employment of Physicians by Hospitals, and Res. No. 26 on Hospitals Practicing Medicine: These resolutions were given thorough discussion and consideration. All three of these resolutions have to do with the same subject, hospital-physician relationships and methods of payment. Your committee is in full accord with the intent of these resolutions as we understand it. Your committee approves the recommendations of these resolutions and proposes the following substitute resolution embodying the important points:

Resolved, That in the relations of physicians and hospitals, the "Guides for Conduct of Physicians in Relationships with Institutions," as published by the American Medical Association in December, 1951, be strictly followed.

Your committee recommends the adoption of this substitute resolution.

No. 22. Resolution on Memebership Classifications

Dr. W. D. Stovall, Wisconsin, introduced the following resolution, which was referred to the Reference Committee on Amendments to the Constitution and Bylaws:

WHEREAS, Membership classifications within constituent associations greatly vary as to terminology and membership privileges; and

WHEREAS, Membership privileges and obligations common to all state associations would eliminate confusion, promote common practices and provide for an equal basis on which to determine American Medical Association delegates representation; therefore be it

Resolved, That this House of Delegates refer to its constituent associations for advice a proposal that the Board of Trustees undertake to review this matter and present recommendations intended to provide constituent and component associations with a practical solution to this problem.

No. 29. Resolution on Constituent Association Membership Standardization

Dr. J. P. Culpepper Jr., Mississippi, introduced the following resolution, which was referred to the Reference Committee on Amendments to the Constitution and Bylaws:

WHEREAS, There is a need for standardization of terms used for types of membership in the constituent and component medical societies; and

WHEREAS, There is a need for uniformity in the treatment of transfers in membership from one constituent association to another; and

WHEREAS, There ought to be more uniformity in the probationary period for new members, a common method for the collection of membership dues in the American Medical Association, and a uniform date in the time allowed for delinquency, so that the county, state, and American Medical Association could coordinate their membership policies; now therefore be it

Resolved, That the article in THE JOURNAL of the American Medical Association on page 1179 of the Nov. 28, 1953, issue, which suggests a plan for uniformity in membership between the constituent associations and the American Medical Association be referred in a reprint to the proper officers or committees on constitution and bylaws, requesting that the plan be studied and action taken to bring the membership regulations of the constituent associations into agreement with those of the American Medical Association.

Report of Reference Committee on Amendments to the Constitution and Bylaws

Dr. William L. Benedict, Chairman, submitted the following report, which was adopted:

Your committee has considered the resolutions introduced by J. P. Culpepper Jr. of Mississippi and W. D. Stovall of Wisconsin relative to the classification of membership and offers a substitute resolution as follows:

WHEREAS, There are now 32 classifications used to designate membership in the constituent associations; and

WHEREAS, Representation in the American Medical Association's House of Delegates is based on the constituent association's number of active members, and the type of membership held is therefore extremely important in determining the member's status in the American Medical Association; and

WHEREAS, There is an urgent need for uniformity which would correlate the classes of membership in the constituent associations with membership in the American Medical Association; therefore be it

Resolved, That this House of Delegates approve the plan as outlined in an article on this subject in THE JOURNAL of the American Medical Association for Nov. 28, 1953, and that it authorize the distribution of a reprint of the article to every secretary of a constituent and component medical society, with the suggestion that definite efforts be made toward the standardization of the classifications of membership in the constituent and component medical societies.

No. 23. Resolution on Medical School Training

Dr. George M. Fister, Utah, presented the following resolution, which was referred to the Reference Committee on Medical Education and Hospitals:

WHEREAS, Graduates from medical schools are now inadequately trained in medical ethics, medical jurisprudence, and medical economics; and

WHEREAS, Doctors entering the practice of medicine are handicapped as a result; now therefore be it

Resolved, That the House of Delegates of the American Medical Association recommend that the Board of Trustees offer a yearly prize of a

substantial sum of money to be offered to the medical schools providing the best course in (1) medical ethics, (2) medical jurisprudence, and (3) medical economics.

Report of Reference Committee on Medical Education and Hospitals

Dr. James Z. Appel, Chairman, presented the following report, which was adopted:

Your reference committee received Resolution No. 23 introduced by Dr. George M. Fister of Utah entitled "Medical School Training." Your reference committee believes it undesirable to offer a prize to medical schools, and therefore recommends a substitute resolution, as follows:

Resolved, That the House of Delegates recommend that the Board of Trustees and the Council on Medical Education and Hospitals continue to stimulate all medical schools of the country to provide courses in medical ethics, medical jurisprudence, and medical practice and problems.

Your reference committee recommends the adoption of this substitute resolution.

No. 25. Resolution on Representatives to Joint Commission on Accreditation of Hospitals

Dr. Warren W. Babcock, Michigan, introduced the following resolution, which was referred to the Reference Committee on Medical Education and Hospitals:

WHEREAS, The interests of the medical profession and their patients are best served by the mutual cooperation of all physicians; and

WHEREAS, Specialty groups have the privilege of naming representatives to the Joint Commission for the Accreditation of Hospitals; now therefore be it

Resolved, That the Michigan State Medical Society request its delegates to the American Medical Association to recommend that the American Academy of General Practice be accorded the same privilege and that the Board of Trustees of the American Medical Association be requested to permit the American Academy of General Practice to name two of the six American Medical Association representatives to the Joint Commission on Accreditation of Hospitals.

Report of Reference Committee on Medical Education and Hospitals

Dr. James Z. Appel, Chairman, submitted the following report, which was adopted:

Your reference committee received Resolution No. 25 introduced by Dr. W. W. Babcock of Michigan entitled "Representatives to Joint Commission on Accreditation of Hospitals." After consultation with a representative of the Board of Trustees, your reference committee learned that there are two representatives of the American Medical Association on the Joint Commission on the Accreditation of Hospitals who are general practitioners. Further, it is the intention of the Board of Trustees to continue to have at least two general practitioners as part of their representation. Your reference committee believes it is bad precedent to direct the Board of Trustees to permit nominations or appointments by any organization other than included in the structure of the American Medical Association. Your reference committee therefore recommends that this resolution be rejected.

No. 27. Resolution on Gamma Globulin

Dr. Robert W. Kimbro, Texas, introduced the following resolution, which was referred to the Reference Committee on Miscellaneous Business:

WHEREAS, The national policy for the control and distribution of gamma globulin is now limited to one national philanthropic organization and is not generally available to those engaged in the practice of medicine except for specific purposes and with specific limitations for experimental use in limited areas threatened with only one specific disease; and

WHEREAS, A number of physicians have used gamma globulin for several years as an aid in the management of certain infectious complications of allergic disorders, frequently recurring respiratory infections, particularly in children, and for other nonspecific conditions; and

WHEREAS, Since the introduction of a control program, gamma globulin is not available for use in these circumstances, and the individual physician is no longer allowed to exercise his own judgment in the administration of this biological; and

WHEREAS, It is believed that the public interest would be better served by a more liberal distribution of gamma globulin; now therefore be it

Resolved, That the American Medical Association recommend that the national policies relative to the distribution of gamma globulin be reevaluated; that the National Foundation for Infantile Paralysis be requested to discontinue the purchase of gamma globulin produced by the commercial houses; and that this gamma globulin be released for normal distribution.

Report of Reference Committee on Miscellaneous Business

Dr. H. Gordon MacLean, Chairman, presented the following report, which was adopted:

Res. No. 27 on Gamma Globulin: It was brought out in evidence before your reference committee that the difficulty of obtaining gamma globulin for the treatment of diseases other than poliomyelitis will resolve itself, for three main reasons (1) that there will be a surplus of gamma globulin from 1953, (2) that there will be new methods of procuring gamma globulin, and (3) that poliomyelitis vaccine will, in all probability, supplant the need for gamma globulin in the prevention of poliomyelitis. For these reasons your committee feels there is no need for this resolution and recommends that it be not adopted.

No. 30. Resolution on Chiropractic Treatment of Crippled Children

Dr. William Weston Jr., South Carolina, introduced the following resolution, which was referred to the Reference Committee on Hygiene and Public Health:

WHEREAS, It has come to the attention of the Medical Society of South Carolina that chiropractors are attempting to operate clinics and to engage in the treatment of crippled children under the auspices of crippled children's societies of certain states; therefore be it

Resolved, That the American Medical Association investigate this condition and advise the various states as required, and that they condemn the chiropractic treatment of cerebral palsy cases under the crippled children's societies' programs if and wherever this exists.

Report of Reference Committee on Hygiene and Public Health

Dr. Thurman B. Givan, Chairman, submitted the following report, which was adopted:

Res. No. 30 on Chiropractic Treatment of Crippled Children: Your committee accepts this resolution with the following changes: That the American Medical Association condemn chiropractic or other cult treatment of cerebral palsy cases under the programs of crippled children's societies wherever they exist. It is the opinion of your committee that any investigation of this situation should be carried out at the local level.

No. 31-A. Resolution on Malpractice Insurance Premiums

Dr. William H. Halley, Colorado, introduced the following resolution, which was referred to the Reference Committee on Insurance and Medical Service:

WHEREAS, Individual members are much concerned about the constantly increasing rates being charged for physicians' liability (malpractice) insurance premiums; now therefore be it

Resolved, That the House of Delegates requests the Board of Trustees of the American Medical Association to investigate thoroughly both the reasons for these constantly increasing premium rates and the possibilities for bringing about a reduction in these rates.

Report of Reference Committee on Insurance and Medical Service

The report of the reference committee on Resolution No. 31-A is contained in its report on the report of the Council on Medical Service on page 1547 of THE JOURNAL, Dec. 26, 1953.

No. 31. Resolutions on Death of Dr. Joseph F. Londrigan

Dr. Elmer P. Weigel, New Jersey, introduced the following resolutions, which were adopted by a unanimous rising vote, without referral:

WHEREAS, The Medical Society of New Jersey was recently bereaved through the death of its distinguished and beloved member and former president, Dr. Joseph F. Londrigan; and

WHEREAS, For many years Dr. Londrigan rendered exemplary service as a member of the New Jersey delegation to the American Medical Association; and

WHEREAS, He would have attended this session to round out the term of his services had not death intervened; therefore be it

Resolved, That the House of Delegates of the American Medical Association record its grief at his passing by standing in silence for one minute in reverent memory; and be it further

Resolved, That a copy of this resolution be spread upon the minutes of this meeting.

Motion on Tape Recording of Proceedings in House

The Speaker announced that a request had been received from one of the constituent associations to make a tape recording of this meeting of the House of Delegates, including the reports of reference committees and all discussions.

Dr. Hugh H. Hussey, District of Columbia, moved that the permission requested be granted. The motion was seconded by several and, after discussion, was lost.

Remarks of Dr. Howard A. Rusk

Dr. Howard A. Rusk, of the Rehabilitation Mission to Korea for the American-Korean Foundation, was introduced by the Speaker and offered the following remarks:

Mr. Speaker and Gentlemen: I appreciate the privilege of giving you this progress report. You were kind enough to let me speak for a few minutes before your meeting in June to tell you something about the health situation and that of our colleagues in Korea. Since that meeting, I have been back to Korea on a second mission. I conveyed to them the feelings of their colleagues in America and gave them a copy of a resolution that you passed at the June meeting. I can not express to you adequately what it meant to the Korean doctors to know the feeling of their colleagues here in America, and today I bring you a message from them of deepest gratitude.

It is particularly pertinent that this report be made to you this morning, because, as you know, four days ago they had the most disastrous fire at Pusan that there has ever been in that country. A city of 250,000 swollen to 1,250,000 refugees, where a fire broke out that burned a mile and one-half strip a half mile wide through the middle of the city, which made homeless more than 300,000 people and destroyed 3,000 houses. You have seen in the press, as of yesterday, what the G. I.'s are doing to help these homeless people, but this morning I want to tell you what our profession has done in the last eight months for Korea.

Upon the plea of the American Korean Foundation, in connection with the need for books, the physicians of America sent to Korea more than 8,000 books. There is still a great need for textbooks and periodicals after 1950 that, if sent to the Alameda Army Depot collect, the American Foundation and the Army will send on to Korea. In addition, the World Medical Association has made available to Korea, through the pharmaceutical houses, enough of their current publications for every doctor to have one. In addition, they have made a substantial monetary contribution to reestablish the national medical society of Korea. In addition, the pharmaceutical houses of America through our foundation have given more than one million dollars worth of drugs and pharmaceuticals in the last eight months, which we have shipped to Korea and certain critical items are going out in the next day or two to meet the needs after the fire. On our mission in Korea in August, we established the first public health school ever established in Korea, and within thirty days after it was established the first class of 30 doctors came in for graduate training. We have also been able to establish a control council for tuberculosis headed by young Korean doctors trained in this country, and one for leprosy, and we have set up a national program for nurses' training.

My reason for remaining here this morning is to say publicly thank you for all the physicians have done, and to bring out one idea that I wonder if our profession might not be interested in. The average doctor in Korea makes about $70 a month. In an inflated economy, much more inflated than we are here, you see how impossible it is to live. Most of them have not had a new suit of clothes for at least five years. The teaching profession, the school teachers, recognizing this need, last year set about in their own organization to raise funds to buy a new suit of clothes, or a new dress, for every teacher in Korea —not the actual dress and the suit of clothes but cloth and the findings. We now have raised among the teachers of America some $80,000, enough for a new suit or a new dress for every teacher in Korea. What it has done for their morale you might well realize. Our foundation hopes to set up a similar program for doctors. It costs about $20 for a suit of clothes. We shall announce it in the appropriate journals, but I thought I would like to tell you about our idea which will be a part of our attempt to help Korea help itself.

Thanks again for all that you have done, in behalf of the Korean doctors as well as those of us of the Foundation.

No. 32. Resolution from Executive Committee of Section on Military Medicine

Permission was requested by the delegate of the Section on Military Medicine, Dr. Russel V. Lee, for the introduction of a Resolution on Medical Military Scholarships. The request was referred to the Reference Committee on Medical Military Affairs for determination as to its emergency nature.

Report of Reference Committee on Medical Military Affairs

Dr. William A. Hyland, Chairman, presented the following report, which was adopted:

Your reference committee recognizes the urgency of this resolution. However, in view of the significance of the subject and the need for thorough consideration, it is recommended that the House of Delegates not act on the resolution during this session, but that it be referred to the Board of Trustees for prompt and careful study and action.

No. 33. Resolutions on Death of Dr. Joseph H. Howard

Dr. Stanley B. Weld, Connecticut, introduced the following resolutions, which were adopted by unanimous rising vote, without referral:

WHEREAS, In the death of Dr. Joseph H. Howard of Bridgeport, Conn., in September of this year American medicine has lost one of its most courageous and enthusiastic statesmen and the medical profession of Connecticut a leader of outstanding ability; and

WHEREAS, Dr. Howard, an eminent gynecologist and obstetrician, was a member of the House of Delegates of the American Medical Association for the past eight years, a past president of his county and state medical societies and a member of many allied organizations where his counsel and judgment were sought during all the 30 years of his membership in organized medicine; therefore be it

Resolved, That the House of Delegates of the American Medical Association in session in St. Louis Dec. 1 to 3, 1953, expresses its deep sense of loss in the death of Dr. Howard; and be it further

Resolved, That a copy of this resolution be sent to the family of the deceased.

Report of Reference Committee on Credentials

Dr. Walter E. Vest, Chairman, presented the following report, which, with the exception of Recommendation 10, was adopted:

Your Reference Committee on Credentials met three times and offers the following report:

One hundred and seventy-eight delegates have been seated so far this session.

Your committee believes that the House of Delegates of the American Medical Association is the greatest deliberative medical body in the world, and that the decisions arrived at in its sessions set the patterns for medicine now and provide the guideposts for medicine-to-be for the entire predictable future. It behooves the House of Delegates, therefore, to be sure of the credentials of every member seated and to have documentary evidence in the committee files to justify the seating of every member admitted. Your committee believes also that the legality of the transactions of this body might possibly be called in question if an individual should be seated and vote, and it should develop later that he had no legal right to membership, certainly if the vote were close. Approximately a dozen members of this House presented either faulty credentials or none, and your committee feels this is too high a percentage. The representative from one state, an alternate this year and a duly elected delegate for 1954, presented no credentials, apparently through no fault of his own. Your committee voted to seat him, and the president of his society has since confirmed his eligibility to membership by telegram.

In order to expedite the work of the House of Delegates at future sessions and especially to simplify and expedite the work of the Reference Committee on Credentials your committee offers the following recommendations:

1. That hereafter only those individuals presenting documentary evidence of the right to membership in the House of Delegates satisfactory to the Credentials Committee for deposit in the committee files be seated.

2. That the Credentials Committee be furnished by the headquarters office not only an official list of delegates but a separate official list of alternate delegates as well.

3. That a supply of blank credentials cards be available.

4. That the desk for filling out House of Delegates register slips be plainly marked and, where physical facilities admit, that this desk be aligned with the committee's desks.

5. That one entirely separate desk, suitably marked, be set up for the registration of alternate delegates and that this desk be manned by employees of the American Medical Association rather than by members of the House of Delegates.

6. That the Credentials Committee's desks, instead of being marked with letters as at present, be marked "Alabama to Montana," and "Nebraska to Wyoming, Territories and Sections."

7. That two rubber stamps bearing the words "Credentials Accepted" be furnished the Credentials Committee.

8. That with the Secretary's letter to prospective members of the House of Delegates a slip be enclosed on which is printed in bold capitals, preferably in red ink, the following: Be Sure to Read "Your Role as a Delegate;" Be Sure to Bring Your Credentials; Be Sure to Present This Slip with Your Credentials. This slip can be stamped "Credentials Accepted" and presented for badges and House of Delegates folders and badges and folders given to members only on presentation of this slip properly stamped.

9. That badges and House of Delegates folders be given out together.

10. That a separate door be marked for the admission of delegates and that this door be locked as soon as the House is called to order and thereafter delegates and visitors alike be required to use the general entrance at the rear of the meeting room.

11. That at least two members of the Credentials Committee be appointed from the membership of its immediate predecessor.

12. That the Secretary of the Association be authorized to disregard any of these suggestions he deems impractical.

No. 34. Resolutions on Voluntary Health Insurance

Dr. Percy E. Hopkins, Illinois, introduced the following resolutions, which the Speaker announced the Reference Committee on Insurance and Medical Service had declared to be of an emergency nature, and which were adopted unanimously:

On Dec. 2, 1953, the Council on Medical Service received information from the Committee on Prepayment Medical and Hospital Service, which, in the opinion of the Council, demands immediate action by the House of Delegates of the American Medical Association. Therefore, the following resolutions are presented:

WHEREAS, Health Service, Inc., a capital stock casualty insurance company reported to be wholly owned by the Blue Cross Commission of the American Hospital Association, has issued insurance contracts to employees of the meat packing industry and their dependents in violation of the principles established by the American Medical Association; and

WHEREAS, Health Service, Inc. and other insurers may issue other similar contracts; and

WHEREAS, The issuance of these contracts is evidence of continued disregard of the principles as set forth by the House of Delegates of the American Medical Association, which principles define pathology, radiology, anesthesiology, and physiatry as medical services; and

WHEREAS, This continued disregard becomes even more disturbing in view of the fact that Medical Indemnity of America, Inc., an insurance company said to be owned and controlled by Blue Shield Medical Care Plans, Inc., and Health Service, Inc., are operated under an agreement whereby each insurer assumes half of the risk underwritten by the other; and

WHEREAS, The American Medical Association is concerned with all branches of medicine as they relate to the health of American citizens and recognizes that insurance plans of this type will result in lowering the quality of medical care; therefore be it

Resolved, That the American Medical Association condemns all insurance contracts which classify any medical service as a hospital service; and be it further

Resolved, That the House of Delegates in session on Dec. 3, 1953, reaffirms all past actions of the House of Delegates relating to the subject, which actions are compatible with the following:

With respect to hospital expense benefit insurance the House at its 1937 Annual Meeting in Atlantic City stated: "The subscribers' contract should exclude all medical services—contract provisions should be limited exclusively to hospital facilities. If hospital service is limited to include only hospital room accommodations such as bed, board, operating room; medicines, surgical dressings, and general nursing care, the distinction between hospital service and medical service will be clear."

In 1950 at the Cleveland Clinical Session the House amplified its position as follows: "The hospital benefits should include bed, board, general nursing, operating and obstetrical room services, dressings, and medications while in the hospital. Electrocardiographic, metabolic, roentgenographic, pathology studies, anesthesia, and physiotherapy should be included in the medical insurance benefits and not in the hospital contract.

"The patient should have a free choice of physician regardless of the insurance plan purchased or provided."

Again, at its 1951 Clinical Sesion in Los Angeles the House redefined certain medical practices in the following words:

"Past actions of the House of Delegates give every reason to reiterate that radiology, anesthesiology, pathology, and physiatry constitute the practice of medicine;" and be it further

Resolved, That copies of this resolution be sent to Health Service, Inc., Medical Indemnity of America, Inc., Blue Cross Commission, Blue Shield Medical Care Plans, Inc., The Health Insurance Council, and other insurance organizations which have issued or may issue contracts in conflict with these resolutions.

Report of Reference Committee on Rules and Order of Business

Dr. Joseph B. Copeland, Chairman, presented the following report, which was adopted:

Your Reference Committee on Rules and Order of Business, acting for the House of Delegates, wishes to make some brief motions expressing commendation and appreciation to various persons and organizations whose efforts have contributed so much toward making this meeting successful.

1. Your reference committee moves that a sincere vote of thanks and appreciation be extended to the Local Committee on Arrangements under the able chairmanship of Dr. Llewellyn Sale, and to the Subcommittee on Woman's Auxiliary to the St. Louis Medical Society under the chairmanship of Mrs. Theodore Greiner.

2. To the Secretary's Office and staff under the capable direction of Mrs. Cascio and to the Public Relations Bureau and staff of the headquarters office.

3. To the Missouri State Medical Association and the St. Louis Medical Society.

4. To the city of St. Louis and the St. Louis Convention and Publicity Bureau headed by Mr. Fred Rein.

5. To the Jefferson Hotel, its management and staff, especially Mr. Dix.

6. To the Michigan State Medical Society and the Michigan Medical Service and to the Aces and Deuces, for the luncheons these groups gave for the House of Delegates.

7. To the Speaker and Vice Speaker of the House of Delegates for their usual fair and judicial handling of the proceedings of the House.

The House of Delegates adjourned sine die at 3 p. m., Thursday, Dec. 3, 1953.

PHYSICIANS REGISTRATION
CLINICAL MEETING, ST. LOUIS, DEC. 1-4, 1953

Alabama	18
Arizona	2
Arkansas	31
California	52
Colorado	23
Connecticut	12
Delaware	4
District of Columbia	24
Florida	8
Georgia	9
Hawaii	1
Idaho	7
Illinois	506
Indiana	91
Iowa	60
Kansas	38
Kentucky	38
Louisiana	18
Maine	2
Maryland	15
Massachusetts	24
Michigan	59
Minnesota	58
Mississippi	15
Missouri	1,040
Montana	8
Nebraska	25
Nevada	2
New Hampshire	3
New Jersey	21
New Mexico	4
New York	70
North Carolina	7
North Dakota	9
Ohio	114
Oklahoma	31
Oregon	9
Pennsylvania	32
Puerto Rico	1
Rhode Island	3
South Carolina	6
South Dakota	5
Tennessee	37
Texas	71
Utah	8
Vermont	1
Virginia	18
Washington	16
West Virginia	9
Wisconsin	43
Wyoming	5
Total	2,712

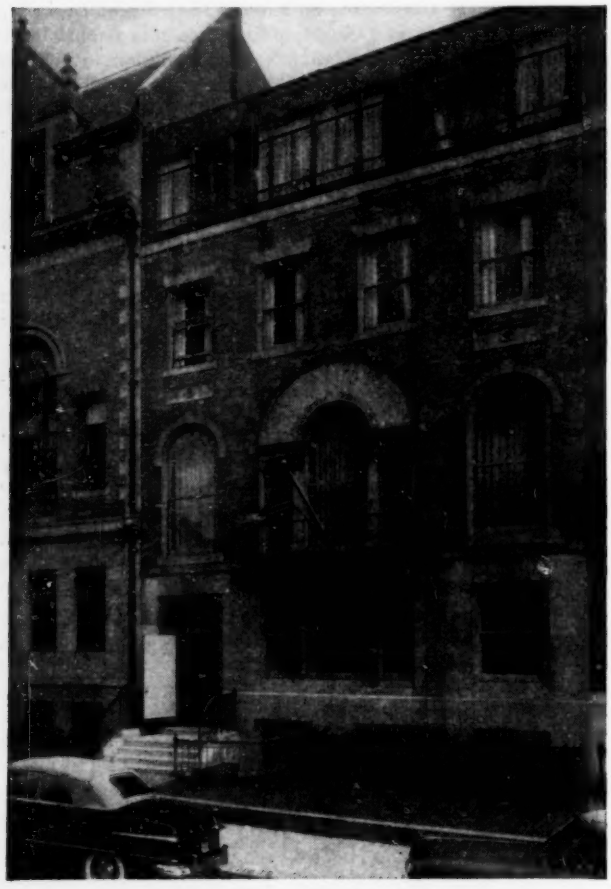
Other Countries

Canada	4
England	2
India	2
Israel	1
Korea	2
Norway	1
Pakistan	2
Philippines	2
Thailand	1
Uruguay	1
Total	18
Grand Total	2,730

MASSACHUSETTS STATE MEDICAL SOCIETY

To permit readers of THE JOURNAL *to become better acquainted with the activities of state medical associations articles describing them will appear from time to time in these pages.*—ED.

Having the distinction of being the oldest medical society in the United States with a continuous existence, the Massachusetts Medical Society is first in THE JOURNAL'S series on medical societies affiliated with the American Medical Association. Fourteen founders were listed in the bill for incorporation of the present society, read for the first time to the legislature on May 11, 1781. About half a year later (Nov. 1) when Gov. John Hancock signed the charter act, 31 incorporators were listed. Other but short-lived medical societies had appeared earlier. The first such society was formed in Boston in 1735; the second was "A Society of Gentlemen in New York, Founded About 1749 for the Weekly Discussion of Medical Subjects"; and the third was the Philadelphia Medical Society, founded in 1765. In the same year Cotton Tufts of Weymouth tried to organize a state medical society, and the following year, on July 23, 1766, the Medical Society of New Jersey came into being, but for an interrupted course, its meeting being suspended from 1775 to 1781 and from 1795 to 1807.



Headquarters of Massachusetts State Medical Society.

The Massachusetts Medical Society held its first meeting Nov. 28, 1781, in the County Court House, Boston. By 1803 it had acquired a membership of 67. In the 150 intervening years, 172 years after its founding, the society has expanded to its present membership of 7,191 physicians in 19 district medical societies, with a woman's auxiliary of 2,000 members. Its headquarters building at 22 The Fenway in Boston, a four-story structure with basement and sub-basement facilities, houses the offices of the president, secretary, treasurer, executive secretary, and director of medical information and education; the recently incorporated Postgraduate Medical Institute; an auditorium-type meeting room seating 49; and two smaller committee rooms. Two additional auditoriums are available for use by the society in the Boston Medical Library, which is located next door and which contains the editorial offices of the weekly *New England Journal of Medicine*, the official organ of the Massachusetts and New Hampshire medical societies. Headquarters facilities of the Massachusetts Medical Society are made available to allied medical and health groups, and a central clearing house of all available information concerning postgraduate medical education in the state was set up in 1951 as a service to physicians in cooperation with the medical schools of Harvard University, Boston University, and Tufts College; the Lahey and Joslin clinics; the Massachusetts Heart Association; the Tuberculosis and Health League; the Academy of General Practice; and the National Foundation for Infantile Paralysis. In cooperation with the medical societies of New England, the society conducts the annual three day New England Postgraduate Assembly. Officers of the society for the current year are: president, Dr. Frederic Hagler; president-elect, Dr. Curtis C. Tripp; vice-president, Dr. Harvey A. Kelly; secretary, Dr. Robert W. Buck; treasurer, Dr. Eliot Hubbard Jr., and assistant treasurer, Dr. Norman A. Welch. Dr. John F. Conlin is director of medical information and education, and Mr. Robert St. B. Boyd serves the association as executive secretary.

THE SCIENTIFIC EXHIBIT AT THE ST. LOUIS CLINICAL MEETING

The Scientific Exhibit at the Clinical Meeting in St. Louis was acclaimed by numerous physicians as an outstanding contribution to graduate medical instruction. The spaciousness of the hall permitted a dignity not often attainable, while the artistic efforts of numerous contributors resulted in a group of exhibits that were delightful. The exhibit symposium on prevention of traffic accidents was a timely subject, exciting much attention including that of police officers and judges of traffic courts. The special exhibit on fractures was as popular as ever. An added feature this year was a consultation service, where physicians could discuss their problems with a group of experts. Manikin demonstrations on problems of delivery, which were presented several times each day, resulted in unexpectedly large audiences that overflowed the space available. The question and answer conference on diabetes was conducted in a small room adjacent to the exhibit on the same subject. The room was filled to capacity at all times.

There were 78 other exhibits, grouped for the most part according to subject discussed in the clinical lectures, including surgery, obstetrics and gynecology, internal medicine and therapeutics, arthritis and rheumatism, cardiovascular diseases, pediatrics, pulmonary diseases, gastrointestinal diseases, neurology and psychiatry, and miscellaneous subjects. The careful preparation of these exhibits, together with the conscientious demonstration by their authors throughout the week, supplemented the lectures on the same subjects and added much to the value of the meeting. An acknowledgment of gratitude is made to the numerous physicians and scientists who contributed so much of their time and energy in helping to make the meeting a success.

Motion pictures were shown at hours that did not conflict with the lecture program of the section groups. The films were carefully selected for their general interest by the Committee on Medical Motion Pictures. In addition to the regular program, a three-dimension film was shown each day in another area. On Wednesday evening, an outstanding group of films was presented at the Statler Hotel. The capacity audience, together with the laudatory comments, encourages the extension of such an evening attraction. The Committee on Scientific Exhibit expresses appreciation to the chairman of the local committee on arrangements and to all members of the subcommittees for their willing cooperation.

NEW A. M. A. PUBLICATION

Conference on Veterans' Medical Care.—This pamphlet comprises a summary of the conference on veterans' medical care held in Chicago, Sept. 1, 1953, and sponsored by the Committee on Federal Medical Services, Council on Medical Service, American Medical Association.

MEDICAL NEWS

ALABAMA

Hospital News.—The State Building Commission has allocated 1 million dollars for improvements at Alabama mental institutions. Bryce Hospital at Tuscaloosa was allotted $805,000 for a new building and $100,000 for renovation and improvement of present facilities. Searcy Hospital, Mount Vernon, was given $80,000, Partlow State School, Tuscaloosa, $15,000, and the Institute for the Deaf and Blind at Talladega, $70,000 for a new dormitory, $50,000 for a shop building, and $80,000 for improving present buildings.

Personal.—Dr. French H. Craddock Sr., medical director of the Drummond-Fraser Hospital, Sylacauga, was recently named vice-president of Avondale Mills in recognition of his long service record with the company. He will continue as medical director of the hospital.——Dr. Roger D. Baker, professor of pathology, Medical College of Alabama, Birmingham, since 1944, has been appointed professor of pathology at Duke University School of Medicine, Durham, N. C., and chief of pathology at the VA Hospital in Durham.——Dr. Robert H. Watson, Georgiana, was recently honored when a loving cup was presented to him in appreciation of his more than 50 years of service to the community.——Dr. James L. Hardwick, a veteran of World War II, was recently elected mayor of Talladega.

CALIFORNIA

Study of Insect Disease Vectors.—The School of Tropical and Preventive Medicine, College of Medical Evangelists, Loma Linda, recently built a mobile laboratory unit, mounted on a four-wheel-drive jeep chassis, which will be used for an expedition to Mexico to study insect disease vectors.

Meeting on Bacterial Infections.—The Los Angeles Society of Internal Medicine will meet Jan. 6 in the lounge of the Los Angeles County Medical Association. Guests are welcome for the 8 o'clock program, in which Dr. W. Barry Wood Jr., head, department of medicine, Washington University School of Medicine, St. Louis, will present "Studies on the Cellular Immunology of Acute Bacterial Infections."

Society-Sponsored Arts Center.—At the annual San Joaquin County Fair, the San Joaquin County Medical Society sponsored a Medical Arts Center. The exhibitors were the American Cancer Society, National Tuberculosis Association, American Heart Association, local health district, American Red Cross, St. Joseph's Hospital, National Society for Crippled Children and Adults, National Foundation for Infantile Paralysis, and the medical society. The medical center included displays depicting the work of each of these organizations.

Mass Distribution of First Aid Charts.—Through the joint effort of the Los Angeles *Times* and the Los Angeles County Medical Association, 750,000 local residents were offered a first aid chart that was reproduced in full on the editorial page of the *Times*, and accompanied by a signed article by Dr. Paul D. Foster, president, Los Angeles County Medical Association, urging readers to clip out the chart and paste it on the inside of their medicine cabinets. The enthusiastic response to the chart has resulted in plans to give it even broader circulation. Lockheed Aircraft has reproduced it in a plant publication that reaches 60,000 employees. Copies of the chart printed on cardboard in red and white are available at cost, $2.10 per hundred. Phone DUnkirk 5-1581, or write to 1925 Wilshire Blvd., Los Angeles 57.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

COLORADO

Home for Asthmatic Children.—The National Home for Jewish Children at Denver, which has at the core of its program the free, nationwide treatment of needy children suffering from chronic intractable asthma, has changed its name to the Jewish National Home for Asthmatic Children. The institution first opened in 1907 as a "sheltering home" for dependent children of the tuberculous poor. In 1940 the home launched its research program devoted to the child with asthma. Since then it has given completely free treatment to children from practically every state in the Union. The American Medical Association recently presented a research grant to Dr. Allan Hurst of the home to further studies of pulmonary functions in children. Dr. M. Murray Peshkin, New York, president of the American College of Allergists, is chief national medical consultant to the home.

CONNECTICUT

Tumor Clinics' Award.—The Association of Connecticut Tumor Clinics announces the second annual competition for the award for the best paper on cancer submitted by any licensed physician in Connecticut. First prize is $100 and second prize, $50. Preference will be given to papers relating to the results of treatment of cancer based on studies utilizing the tumor records of the Connecticut hospitals. All entries must be sent to the secretary, Association of Connecticut Tumor Clinics (Dr. Robert Tennant, 80 Seymour St., Hartford 14) on or before March 1.

Lectures on Monday Evenings.—The Hartford Medical Society announces a series of lectures on Mondays at 8:30 p. m. in the Hunt Memorial Building, Hartford, following a 5 o'clock clinical conference at one of the local hospitals:

Jan. 18, Practical Approach to Treatment of Anxiety, Joseph F. Hughes, Philadelphia.
Feb. 1, Surgical Treatment of Pancreatic Disease, Richard B. Cattell, Boston.
Feb. 15, Some Problems Associated with Major Catastrophes, Isidor S. Ravdin, Philadelphia.
March 1, Diagnosis and Management of Diseases of the Aseptic Meningitis Type, Theodore E. Woodward, Baltimore.
March 15, Clinical Disturbances Produced by the Overfunction and Underfunction of the Pituitary Gland, Edward H. Rynearson, Rochester, Minn.
April 5, Angiography, Israel Steinberg, New York.
April 19, Indications for Surgery in Valvular Heart Disease: With Specific Reference to Mitral Stenosis, Edward F. Bland, Boston.

DISTRICT OF COLUMBIA

University News.—Dr. Robert P. Nenno, formerly assistant professor of psychology at the College of St. Thomas, St. Paul, has been appointed assistant professor of psychiatry at the Georgetown University School of Medicine, Washington.

Donation of Slides of Breast Tumors.—Dr. Max Cutler, Los Angeles, recently donated to the Armed Forces Institute of Pathology, Washington, D. C., the collection of large slides of breast tumors, which formed a basis for the monograph by Drs. G. L. Cheatle and M. Cutler, "Tumours of the Breast: Their Pathology, Symptoms, Diagnosis and Treatment," London, 1931.

Society Honors Dr. Herbst.—At its annual banquet, the Medical Society of the District of Columbia presented a certificate of meritorious service to Dr. William P. Herbst Jr. "in grateful acknowledgment of his service to the medical profession and to the people of the District of Columbia." Dr. Herbst was president of the society in 1946 and chairman of the executive board in 1951. He is presently chairman of the committee on public policy and a member of the committee on cancer control. One of the organizers of Washington's Blue Shield Plan, Medical Service of the District of Columbia, and a member

of its first board of trustees, Dr. Herbst has been the service's first vice-president since 1950. He is president of the Social Hygiene Society of the District of Columbia, and a member of the executive committee of the District of Columbia Survey of Medical Care of the Indigent and Related Services. He has been president of the Washington Academy of Surgery and the Washington Urological Society, and is a member of the board of trustees of the American Urological Research Foundation and of the governing board of the Committee on Postgraduate Urological Education of the American Urological Association.

IDAHO

Society News.—The Idaho Falls Medical Society elected Dr. Fred E. Wallber, president, Dr. John S. Hatch, vice-president, Dr. L. Stanley Sell, secretary-treasurer, Drs. Wallber and Dauchy Migel, delegates to the state convention, and Drs. Hamilton R. Fishback Jr. and Wendell L. Nielsen, alternates.

ILLINOIS

Fifty Year Club.—Fifty year pins and certificates were recently presented to Dr. Christian H. Zoller, Litchfield, and Dr. George D. Runkle, Stockton. A plaque honoring his 50 years of medical practice in DuPage County was presented to Dr. Edward W. Marquardt, Elmhurst, by the Illinois State Medical Society.

Hospital News.—Dr. Alan Lieberman, clinical director of Elgin State Hospital, retired Nov. 30, 1953, to enter private practice in Elgin. Dr. Lieberman, who has been a state welfare employee for 15 years, will serve as consultant in psychiatry at the hospital. Dr. Werner Tuteur, who has been in state service since 1942, has been named to succeed Dr. Lieberman.

Chicago

R. R. McCormick Foundation.—Col. Robert R. McCormick, editor and publisher of the Chicago *Tribune*, has announced the incorporation of a nonprofit organization that includes among its projects the endowment of free beds at Passavant Memorial Hospital, provision of funds to the hospital for treatment of indigent sick and injured persons, and aid to sick and disabled ex-service men.

Cardiac Conference.—The next regular clinicopathological cardiac conference of Cook County Hospital will be held Jan. 8, 11 a. m. to 12 noon, in the Children's Amphitheatre, 700 S. Wood St. Dr. Willis J. Potts, surgeon-in-chief, Children's Memorial Hospital, will speak on surgery of congenital malformations of the heart (discussion by Dr. Egbert H. Fell, clinical professor of surgery, University of Illinois College of Medicine). Everyone is invited.

New Plans for Cancer Research.—According to a report from the University of Chicago, Mr. Maurice Goldblatt, chairman of the board of the University of Chicago Cancer Research Foundation, plans to add 1,000 associates, a new class of members, to the foundation. Each of the associates will contribute $100 a year, and will meet with the doctors and scientists at an annual dinner meeting to discuss progress. Organization of the associates will be confined to Chicago at the start. By next spring Mr. Goldblatt plans to add associates from various parts of the country. Mr. Goldblatt, who is a governor of the National Cancer Institute of the U. S. Public Health Service, led a campaign in 1947 that raised $1,200,000 for the university's research facilities.

Rehabilitation Institute.—Dr. Ben L. Boynton, recently appointed professor of physical medicine and rehabilitation, Northwestern University Medical School, has been named director for the new Rehabilitation Institute of Chicago. The institute, a nonprofit organization, is patterned after the New York University-Bellevue Medical Center Institute of Physical Medicine and Rehabilitation but will be a civic undertaking, not operated in connection with any particular hospital or medical school. Its services will be available to all who qualify for rehabilitation, at standard rates established by the institute according to the individual needs of each patient. It will have on its staff consultants in all the medical specialties and a job placement officer to help rehabilitated patients secure work within the limits of their capabilities on a competitive basis among nonhandicapped persons. A team of physicians, sociologists, educators, and physical, occupational, and speech therapists will teach the patient how to make the best use of these capabilities. Among those to whom major credit is given for the organization and establishment of the new institute is Dr. Paul B. Magnuson, who has devoted his time without compensation to the project since completion of his work as chairman of the President's Commission on the Health Needs of the Nation. Dr. Magnuson, who was first medical director of the Illinois Industrial Commission, served as civilian consultant to the chief surgeon of the U. S. Army and was chief medical director of the Veterans Administration in Washington from 1946 to 1951. For 15 years he was professor of surgery at Northwestern University Medical School.

KANSAS

Society News.—The recently organized Kansas State Pediatrics Association has named Dr. Frank L. Menehan, Wichita, president, Dr. Bertrand I. Krehbiel, Topeka, vice-president, and Dr. David R. Davis, Emporia, secretary-treasurer.

Child Psychiatry Fellowship.—The John Harper Seeley foundation, Ann Arbor, Mich., has made funds available to establish the first graduate fellowship in child psychiatry at the Menninger Foundation. Dr. Povl Toussieng, the first fellow in this new program, will spend his two year training period at the Southard School. Dr. Toussieng, who received his medical degree from the University of Copenhagen, Denmark, in 1945, came to the United States as an exchange student in 1949 and, after an internship at St. Joseph's Hospital in Kansas City, Mo., entered the Menninger School of Psychiatry as a resident at Topeka State Hospital, where he completed his residency in June.

University News.—Dr. C. Frederick Kittle, assistant professor of surgery, University of Kansas School of Medicine, Kansas City, is spending several months in Europe. He will visit centers where cardiac and other thoracic surgery is being done. The Markle scholarship awarded to Dr. Kittle provides the opportunity for this period of study abroad.——An intramural research grant program has been established at the Kansas University Medical Center, Kansas City, to supplement present departmental programs supported by developmental funds. Its chief purpose is to encourage research by medical students, interns, residents, and junior staff members by providing amounts up to $500 to individuals for research projects. Grants will be made only on an annual basis, subject to continuation at the termination of the period for which each grant has been made.

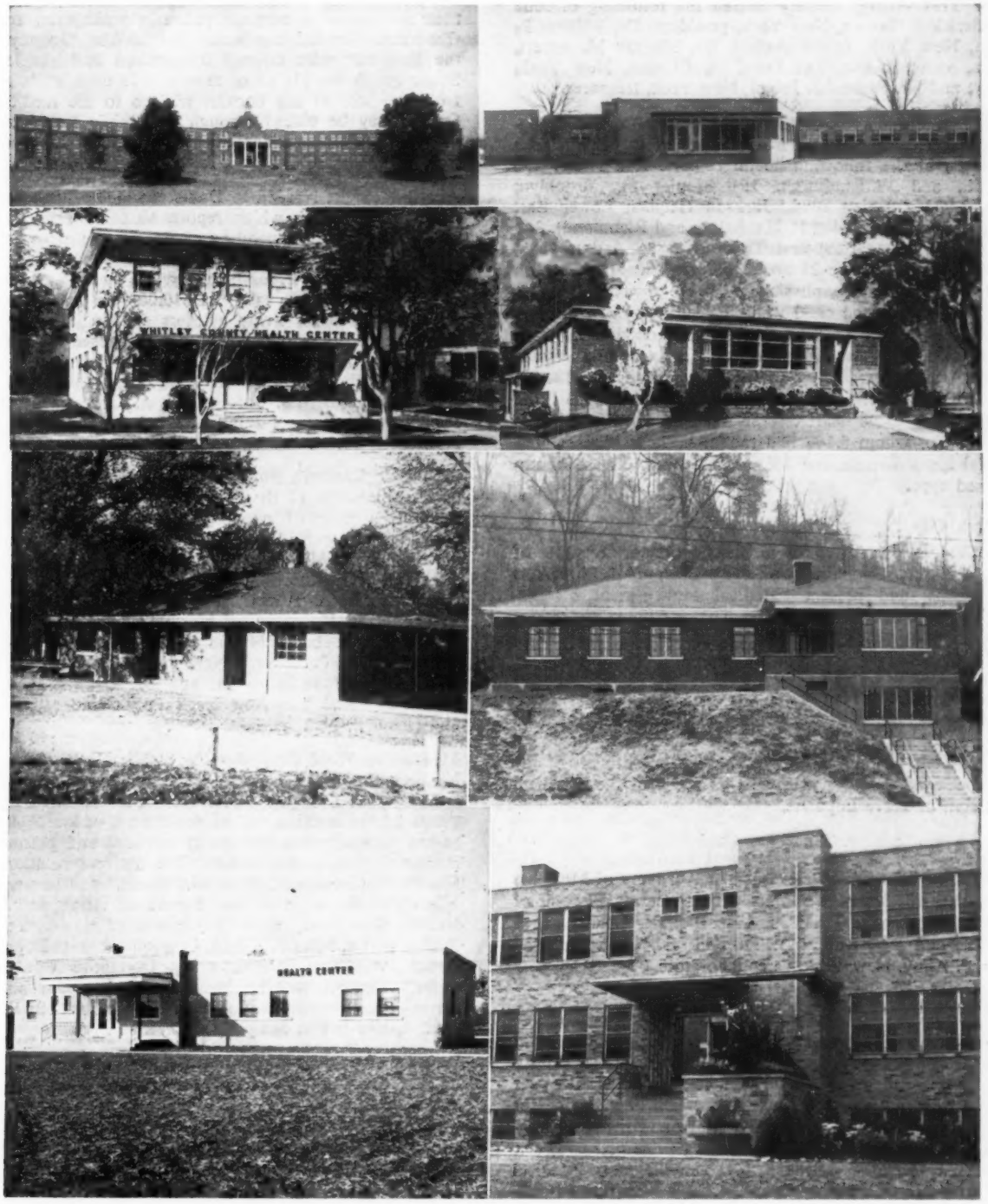
KENTUCKY

University News.—Special grants for research and teaching projects to the University of Louisville School of Medicine total $366,815 for 1953, the highest figure ever recorded for one year's financial aid in the school's history, according to Dr. J. Murray Kinsman, dean. The largest of the 19 grants was $40,350 from the National Foundation for Infantile Paralysis.

Radioisotope Laboratory.—A $56,000 radioisotope laboratory to aid in combating cancer and other diseases in Kentucky and Indiana was dedicated Nov. 23, 1953, at Louisville General Hospital. Funds for the unit were provided by the city of Louisville, the cancer division of the state board of health, the Kentucky division of the American Cancer Society, and the University of Louisville, which will use the laboratory. The first patients were admitted Dec. 15 to the isotope unit, which will do research, diagnostic, and therapeutic work.

Kentucky Hospitals Built With Hill-Burton Aid.—The Hill-Burton Act, enacted by the Congress in 1946, authorized the federal government to appropriate funds to the states to assist communities in building hospitals and health centers. The total amount of funds necessary for this purpose is to be raised in part by the local communities themselves and in part by the state governments. What Kentucky has done since the passage of the act is an interesting story, as is that of various other states. THE JOURNAL hopes to be able to relate and illustrate, from time to time, some of these activities in various states.

Previous to the passage of the Hill-Burton Act, Kentucky had only 5,745 beds in its general hospitals and needed 13,106 beds. Then its leaders began planning for hospital construction. To date 21 hospitals, 22 health centers, and 15 additions to existing hospitals have been completed, while 8 hospitals, 2 health centers, and additions to 7 existing hospitals are under construction, and 2 more hospitals are in the planning stage. Kentucky has built not only general hospitals, but mental hospitals, tuberculosis hospitals, chronic disease hospitals, and health centers. The *Bulletin of the Kentucky State Department of Health* for November, 1952, shows that the total cost of this program at that time was $42,523,729.79, of which the local communities provided $19,626,345 and the state $964,349.64. The federal government's part in this total expenditure was $21,933,035.15. The Kentucky *Bulletin* includes many pictures of hospitals, several of which are reproduced herewith.



Kentucky hospitals and health centers. Reading from top and left to right are Louisville Hospital, Scottsville Hospital, Williamsburg Health Center, Harlan Health Center, Boonville Health Center, Pineville Health Center, Somerset Health Center, and Bardstown Hospital.

NEW YORK

Society News.—The Rochester Academy of Medicine will present a symposium on "stroke" Jan. 5, 8:30 p. m., at the academy headquarters, 1441 East Avenue, Rochester.——The Brooklyn Dermatological Society announces the following officers for the 1953-1954 term: president, Dr. Camillo B. Locasto; vice-president, Dr. Harry L. Feigenbaum; and secretary, Dr. Frank D. Jennings Jr.——At its annual meeting Nov. 16, 1953, the New York Allergy Society elected the following officers: Dr. Frederick R. Brown, New York, president; Dr. William B. Sherman, New York, president-elect; Dr. Murray M. Albert, Brooklyn, vice-president; Dr. Leoni N. Claman, New York, secretary; and Dr. Samuel J. Prigal, New York, treasurer.

Cardiac Consultation for Children.—The New York City Department of Health operates five cardiac consultation clinics for children at the following health centers: Red Hook, 250 Baltic St., and Williamburgh, 151 Maujer St., Brooklyn; Corona, 34-33 Junction Blvd., Jackson Heights; Lower East Side (serving children living in Manhattan and Richmond), 341 East 25th St., Manhattan; and Tremont, 1826 Arthur Ave., Bronx. Persons up to age 21 are eligible for these services on referral by their private physicians or by physicians in the department's school and child welfare health services. Patients are seen by appointment only. Of the 6,668 children referred to cardiac consultation clinics in 1952, 50.4% had disease diagnosed as noncardiac; 16.6%, potential heart disease; 12.8%, possible heart disease; and 2%, possible and potential heart disease. Organic heart disease was diagnosed in 17% of the patients, of whom 8.1% had rheumatic heart disease, 7% congenital heart disease, and 2% organic heart disease of undetermined type.

New York City

Tumor Clinic.—Dr. Alfred A. Gellhorn, director, Institute of Cancer Research, Columbia University College of Physicians and Surgeons, will present "Medical Management of Disseminated Neoplastic Disease" at the Tumor Clinic Conference, Harlem Hospital, Jan. 20, at 10:45 a. m.

Dr. Loewi Honored.—Dr. Otto Loewi, research professor of pharmacology at the New York University College of Medicine, has been made an honorary member of the Medical Board of the Myasthenia Gravis Foundation. Dr. Loewi, who celebrated his 80th birthday in June, was winner with Sir Harry Dale in 1936 of a Nobel prize for discovery of the chemical transmission of nerve impulses.

OHIO

Symposium on Ulcerative Lesions.—The Academy of Medicine of Cincinnati will present a symposium on ulcerative lesions of the colon, Jan. 5, with Dr. Milton Rosenbaum, Cincinnati, as moderator, and Drs. Rupert B. Turnbull Jr., Cleveland, and Thomas P. Almy, New York, as collaborators.

PENNSYLVANIA

Testimonial to Dr. Cole.—Dr. Lloyd G. Cole, Blossburg, chief surgeon of the Blossburg State Hospital, was tendered a testimonial dinner, Aug. 9, 1953, on completion of his 35th year of service with the hospital. As an expression of gratitude for his untiring interest in community welfare and medical progress, citizens of Blossburg and surrounding areas presented Dr. Cole with a television set, and the Tioga County Medical Society gave him a gavel symbolizing his leadership in medicine and surgery and bearing a silver band inscribed with the notable achievements of his career.

Philadelphia

Newbold Lecture.—The College of Physicians of Philadelphia on Jan. 6, 8:30 p. m., will present the 68th Mary Scott Newbold lecture. Dr. Dickinson W. Richards, Lambert Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, will discuss "Physiologic Behavior and Therapeutic Use of Plasma Volume Expanders."

GENERAL

International Symposium on the Eye.—Following the International Congress of Ophthalmology in New York, next Sept. 13-17, an international symposium on the general physiology and pathology of the eye will be held, Sept. 24-25 at the College of Medicine, State University of Iowa, in Iowa City. All papers and discussions will be in English.

Hospital Booklet for Children.—To familiarize children and their parents with hospital pediatric procedures, the Boston Children's Hospital has issued the booklet "Johnny Goes to the Hospital" with colored illustrations and simple legends. Single copies are $1; six or more are 75 cents each. All profits from the sale of the booklet will go to the medical center. Orders may be placed through the Public Relations Department of the Children's Medical Center, 300 Longwood Ave., Boston 15.

Anesthesiologist Needed in Damascus.—The Institute of International Education, which reports that the Ford Foundation has equipped four operating rooms in the new government hospital in Damascus, is seeking an anesthesiologist to serve in this hospital. The contract with the anesthesiologist will be on a yearly basis at a salary of $10,000 per year plus an allowance of $2,400 for living quarters and an allowance for the shipment of household effects, not to exceed $750 each way. Round-trip travel from New York to Damascus and return will be furnished. Anesthesiologists interested in this position should write to Mrs. Shreve Badger, Department of Special Programs, Institute of International Education, 1 E. 67th St., New York 21.

Lipotropic Research Fund.—Announcement has been received of the formation of the Lipotropic Research Fund, Sept. 16, 1953, by a group of industrial companies. The group plans to encourage the publication of results of such research and to disseminate to the medical profession and other interested scientific groups information relative to the value of the lipotropic substances. It has already alloted grants to Dr. William E. Cornatzer, University of North Dakota, Grand Forks; Dr. Thaddeus D. Labecki, Mississippi State Board of Health, Jackson; Dr. Julius Pomeranze, New York Medical College, Flower and Fifth Avenue Hospitals; and Dr. William B. Rawls, St. Clare's Hospital and New York Poly-Clinic Medical School and Hospital, New York.

Meeting on Weed Control.—The Public Health Section of the Northeastern Weed Control Conference will hold its annual meeting Jan. 6 at the Hotel New Yorker, New York. The theme of the meeting will be the control of weeds detrimental to the public health, principally ragweed and poison ivy. All interested persons are invited. The first presentation, "Public Health Significance of Ragweed Control," will be made by Dr. Miriam Sachs, chief of the Bureau of Adult and Industrial Health, New Jersey State Department of Health, Trenton. At 2:45 p. m. Dr. John F. Kilgus, Connecticut State Department of Health, will discuss "Poison Ivy Dermatitis Control Procedures." Reports will be made on promotional activities in noxious weed control during 1953, public relations in ragweed control, and pollen sampling studies.

World Congress of Cardiology.—The Second World Congress of Cardiology and the scientific sessions of the American Heart Association will be held jointly in Washington, D. C., Sept. 12-17, rather than separately as originally planned. The official title of the congress, previously referred to as the Second International Congress of Cardiology, is the Second World Congress of Cardiology. The scientific sessions and exhibits will be located at the National Guard Armory. The joint scientific program will be presented Sept. 13-17. Opening ceremonies will be held Sunday morning in Constitution Hall, with a reception Sunday afternoon at the Mayflower Hotel. Plans include conducted tours through the National Institutes of Health and the Navy medical center at Bethesda, Md., and the Army medical center, a joint banquet Tuesday evening, and an evening of entertainment, Thursday. Membership will be open to all members of affiliated national cardiological societies and associations throughout the world, and to physicians and other scien-

tists who are interested in the field of cardiology and the circulation. Those desiring to present papers must submit titles and abstracts of not over 200 words in English, and may additionally submit abstracts in one of three foreign languages—French, Spanish or German. Both abstracts and translations must be submitted in duplicate, typed double-spaced with wide margins, and on one side of the sheet only. Abstracts should be sent to the secretaries of the respective national cardiological societies. Abstracts from countries other than the United States must be received at the National Office of the Association, 44 E. 23rd St., New York 10, on or before March 1; abstracts from the United States and Canada, by April 1.

Tape Recorded Medical Abstracts.—The California Medical Association has voted to establish a subsidiary, nonprofit corporation, the Audio-Digest Foundation, to promote "Audio-Digest," a lending library on magnetic tape, originated by Jerry Pettis, public relations man for the association. Through a system of tape recordings and synchronized visual slides or film strips, current medical literature and lectures will be summarized and distributed to physicians throughout the world. Three types of service will be available: 1. A weekly, one hour tape, summarizing current literature (about 600 journals) from the standpoint of significance and practical usage, is designed primarily for the general practitioner. This material is distributed on a subscription basis. Starting Jan. 15, a biweekly, one hour tape will be available for surgeons; a similar service for specialists in internal medicine will be provided starting Feb. 15; and a tape digest for obstetricians and gynecologists, March 15. Taped literature of lectures can be made available in any language. 2. A medical lecture library of on-the-spot recordings made at medical conventions and specially prepared lectures for the Audio-Digest library will be available for purchase or rental. 3. The association is assembling "master" lecture tapes from the leading medical school professors in the nation's 79 medical schools. These tapes, covering the entire field of undergraduate education, will be made available to medical school libraries to supplement local lectures. All lecture material will be reviewed every six months to be kept up to date. Both the taped literature digests and the medical lectures can be duplicated and ready for distribution in less than 24 hours after the master tape has been made.

An annual subscription is $2.75 a week; a 13 week trial subscription is available at $3.25 a week. The recordings are the property of the subscriber. Equipment prices, including special tape recorders equipped for use either in the office or in an automobile, range from $85 to $350. The recorder can also be used for recording case histories, consultations, and reports, as well as for general purpose listening and entertainment in the home. Profits accruing from the Audio-Digest Foundation will be earmarked for the nation's medical schools. Information may be obtained through the California Medical Association, 450 Sutter St., San Francisco 8, or 417 S. Hill St., Los Angeles 13.

EXAMINATIONS AND LICENSURE

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various Centers, July 16. Sec., Dr. Curtiss B. Hickox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* New Orleans, Feb. 2-5 (candidates in south and southwest). Chicago, April 1-3 (candidates in the midwest). Los Angeles, June 15-17 (candidates west of the Rocky Mountains and west coast). The closing date for acceptance of applications for New Orleans, Chicago and Los Angeles will be Jan. 2. New York, Sept. 22-24 (candidates on the east coast). The closing date for acceptance of applications will be April 1). *Written.* Oct. 18. Final date for acceptance of applications will be May 1. *Subspecialties. Cardiovascular Disease.* Chicago, April 1. *Gastroenterology.* Chicago, April 2-3. The closing date for acceptance of applications for the subspecialties will be Jan. 15. Exec. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* Chicago, May or June. Final date for filing application is Jan. 15. Sec., Dr. Leonard T. Furlow, 600 S. Kingshighway, St. Louis 10.

AMERICAN BOARD OF NEUROLOGY AND PSYCHIATRY: *Psychiatry and Neurology.* Chicago, April 29-30. Final date for filing application is Feb. 1. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Written examination (Part I) and review of case histories for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States on Feb. 5. Case abstracts are to be sent by the candidate to the Secretary as soon as possible. Application for reexamination in Part II must be made prior to Feb. 1 of any year. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 25-26, 1954. Final date for filing applications was July 1. *Practical.* San Francisco, June 25-29; New Orleans, Feb. 5-11, 1955. Final date for filing application for 1955 written examination is July 1. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 20-22. Final date for filing application was August 15. Final date for filing application for Part I is Nov. 30. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Boston, May 17-21. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PEDIATRICS: *Written.* Selected Places, Jan. 15. This is the only written examination which will be given during 1954. *Oral.* Washington, D. C., Feb. 19-21; Des Moines, March 19-21; New York City, May 1-3; San Francisco, June 25-27; Chicago, Oct. 8-10 and New Haven, December.

AMERICAN BOARD OF PROCTOLOGY: *Part I.* Kansas City, Philadelphia and San Francisco, May 8. Sec., Dr. Louis A. Buie, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: Chicago, May 10-11. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Spring 1954. Final date for filing application was Dec. 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: *Oral-clinical and pathology.* Chicago, Feb. 17-20. Sec., Dr. Harry Culver, 30 Westwood Road, Minneapolis 16.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country. Feb. 26. Final date for filing application is Jan. 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Street, Detroit, Mich.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1954 Annual Meeting, San Francisco, June 21-25.

1954 Clinical Meeting, Miami, Florida, Nov. 30-Dec. 3.

1955 Annual Meeting, Atlantic City, N. J., June 6-10.

1955 Clinical Meeting, Boston, Nov. 29-Dec. 2.

1956 Annual Meeting, Chicago, June 11-15.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE, Palmer House, Chicago, Feb. 7-9. Dr. Edward L. Turner, 535 N. Dearborn St., Chicago 10, Secretary.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH, Brown Hotel, Louisville, Ky., Feb. 24-25. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

AMERICAN ACADEMY OF ALLERGY, Shamrock Hotel, Houston, Texas, Feb. 1-3. Dr. Alan G. Cazort, 1425 West 7th St., Little Rock, Ark., Secretary.

AMERICAN ACADEMY OF FORENSIC SCIENCES, Drake Hotel, Chicago, Feb. 25-27. Prof. Ralph F. Turner, Michigan State College Dept. of Police Administration, East Lansing, Mich., Secretary.

AMERICAN ACADEMY OF OCCUPATIONAL MEDICINE, John Marshall Hotel, Richmond, Va., Feb. 11-12. Dr. Leonard J. Goldwater, 600 W. 168th St., New York 32, Secretary.

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS, Palmer House, Chicago, Jan. 23-28. Dr. John R. Norcross, 122 S. Michigan Blvd., Chicago 3, Secretary.

AMERICAN COLLEGE OF RADIOLOGY, Drake Hotel, Chicago, Feb. 5. Mr. William C. Stronach, 20 N. Wacker Drive, Chicago 6, Executive Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH:

EASTERN SECTION, Amphitheater, Children's Medical Center, Boston, Jan. 4. Dr. Joseph R. Stanton, 482 Beacon St., Boston 15, Chairman.

SOUTHERN SECTION, Jung Hotel, New Orleans, Jan. 29. Dr. William Parson, University of Virginia School of Medicine, Charlottesville, Va., Chairman.

WESTERN SECTION, Auditorium, University of Oregon Medical School, Portland, Ore., Jan. 28. Dr. I. S. Edelman, University of California Medical Center, San Francisco Hospital, San Francisco 15, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY:

EASTERN SECTION, Waldorf-Astoria, New York, Jan. 8. Dr. Daniel S. Cunning, 118 E. 53d St., New York 22, Chairman.

MIDDLE SECTION, Park Plaza Hotel, St. Louis, Jan. 18. Dr. French K. Hansel, 634 N. Grand Blvd., St. Louis, Chairman.

SOUTHERN SECTION, Brown Hotel, Louisville, Ky., Jan. 16. Dr. William C. Wolfe, 1012 Heyburn Bldg., Louisville 2, Ky., Chairman.

WESTERN SECTION, University of Oregon Medical School, Portland, Ore., Feb. 6. Dr. Guy L. Boyden, 1735 N Wheeler Ave., Portland 12, Ore., Chairman.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Hotel New Yorker, New York, Feb. 11-13. Dr. Marion F. Langer, Room, 303 Lexington Ave., New York 16, Secretary.

AMERICAN PROTESTANT HOSPITAL ASSOCIATION, Palmer House, Chicago, Feb. 10-12. Mr. Albert G. Hahn, Protestant Deaconess Hospital, Evansville, Ind., Executive Secretary.

AMERICAN SOCIETY FOR SURGERY OF THE HAND, Palmer House, Chicago, Jan. 22. Dr. George V. Webster, 960 East Green St., Pasadena 1, Calif., Secretary.

CENTRAL SURGICAL ASSOCIATION, Statler Hotel, Detroit, Feb. 18-20. Dr. Robert M. Zollinger, University Hospital, Columbus 10, Ohio, Secretary.

NORTHWEST SOCIETY FOR CLINICAL RESEARCH, Portland, Ore., Jan. 28. Dr. Arthur L. Rogers, 1216 S.W. Yamhill St., Portland, Ore., Secretary.

REGIONAL MEETINGS, AMERICAN COLLEGE OF PHYSICIANS:
EASTERN PENNSYLVANIA, Philadelphia, Jan. 15. Dr. Thomas M. McMillan, 330 S. Ninth St., Philadelphia 7, Governor.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS: Charlotte, N. C., Hotel Charlotte, Feb. 1-3. Dr. Thomas D. Sparrow, 403 North Tryon St., Charlotte 2, N. C., Chairman.

SOCIETY OF UNIVERSITY SURGEONS, Sheraton Hotel, Rochester, N. Y., Feb. 11-13. Dr. C. Rollins Hanlon, 1325 South Grand Blvd., St. Louis, Secretary.

WESTERN SOCIETY FOR CLINICAL RESEARCH, Portland, Ore., Jan. 29-30. Dr. Herbert N. Hultgren, Stanford Hospital, San Francisco 15, Secretary.

FOREIGN

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND, Leeds, England, May 13-15, 1954. Dr. Henry W. S. Wright, 45 Lincoln's Inn Fields, London W.C.2, England, Honorary Secretary.

BRITISH MEDICAL ASSOCIATION, Glasgow, Scotland, July 1-9, 1954. Dr. A. Macrae, B.M.A. House, Tavistock Square, London, W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Vancouver, B. C., Canada, June 14-18, 1954. Dr. T. C. Routley, 244 St. George St., Toronto 5, Ont., Canada, General Secretary.

CONFERENCE OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, Madrid, Spain, Sept. 26-Oct. 2, 1954. Secretariat, Escuela de Tisiologia, Ciudad Universitaria, Madrid, Spain.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Los Angeles, Calif., U. S. A., Oct. 4-7, 1954. For information write: Dr. T. H. Seldon, 102-110 Second Avenue S. W., Rochester, Minn., U. S. A.

CONGRESS OF INTERNATIONAL ASSOCIATION FOR THE PREVENTION OF BLINDNESS, New York, N. Y., U. S. A., Sept. 12-17, 1954. Professor Franceschetti, 2 Avenue Mirmot, Geneva, Switzerland, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF SURGERY, Paris, France, May 21-22, 1954. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

HEALTH CONGRESS OF THE ROYAL SANITARY INSTITUTE, Scarborough, England, April 27-30. Mr. P. Arthur Wells, Royal Sanitary Institute, 90 Buckingham Palace Road, London, S.W.1, England, Secretary.

INTERNATIONAL CANCER CONGRESS, Sao Paulo, Brazil, July 23-29, 1954. Prof. A. Prudente, 171 rua Benjamin Constante, Sao Paulo, Brazil, President.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS ON CHILD PSYCHIATRY, University of Toronto, Toronto, Ontario, Canada, Aug. 13-14, 1954. Miss Helen Speyer, International Association for Child Psychiatry, 1790 Broadway, New York 19, New York, U. S. A., Executive Officer.

INTERNATIONAL CONGRESS OF CLINICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Dr. Robert A. Moore, Washington University School of Medicine, St. Louis 10, Missouri, U. S. A., Chairman, Committee on Arrangements.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Barcelona, Spain, Oct. 4-8, 1954. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS ON GROUP PSYCHOTHERAPY, Toronto, Ont., Canada, Aug. 12-14, 1954. Dr. J. L. Moreno, Room 327, 101 Park Ave., New York 17, N. Y., U. S. A., Director of Organizing Committee.

INTERNATIONAL CONGRESS OF HEMATOLOGY, Paris, Sept. 6-11, 1954. Dr. Jean Bernard, 86 rue d'Assas, Paris 6e, France, Secretary.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Rome and Salerno, Italy, Sept. 13-20, 1954. For information write: Segreteria XIV Congresso Internazionale di Storia della Medicina, Instituto di Storia della Medicine, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS OF HYDROCLIMATISM AND THALASSOTHERAPY, Dubrovnik, Yugoslavia, May 8-16, 1954. Prof. C. Plavsic, Zeleni venac 1, Belgrade, Yugoslavia, Secretary General.

INTERNATIONAL CONGRESS OF INDUSTRIAL MEDICINE, Naples, Italy, Sept. 13-19, 1954. Professor Scipione Caccuri, Director, Institute of Industrial Medicine Policlinico, Naples, Italy, Chairman, Organizing Committee.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Stockholm, Sweden, Sept. 15-18, 1954. Professor Anders Kristenson, Karolinska Sjukhuset, Stockholm 60, Sweden, Secretary-General.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, São Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF NUTRITION, Amsterdam, Netherlands, Sept. 14-18, 1954. For information write: Dr. M. van Eekelen, Centraal Instituut voor Voedingsonderzoek T.N.O., 61 Catharynesingel, Utrecht, Netherlands.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 26-31, 1954. Dr. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland, President.

INTERNATIONAL CONGRESS OF OPHTHALMOLOGY, University of Montreal and McGill University, Montreal, Canada, Sept. 10-11, 1954, and Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 12-17, 1954. Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minnesota, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF ORTHOPEDIC SURGERY AND TRAUMATOLOGY, Berne, Switzerland, Aug. 30-Sept. 3, 1954. For information write: Professor M. Dubois, Isle-Hospital, Berne, Switzerland.

INTERNATIONAL CONGRESS OF PSYCHOLOGY, Montreal, Canada, June 7-12, 1954. For information write: Prof. H. S. Langfeld, International Union of Scientific Psychology, Eno Hall, Princeton University, Princeton, N. J., U. S. A.

INTERNATIONAL CONGRESS FOR PSYCHOTHERAPY, Zurich, Switzerland, July 21-24, 1954. Dr. H. K. Fierz, Theaterstrasse 12, Zurich 1, Switzerland, Secretary General.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL POLIOMYELITIS CONGRESS, Rome, Italy, Sept. 6-10, 1954. Mr. Stanley E. Henwood, 120 Broadway, New York 5. N. Y., U. S. A., Executive Secretary.

INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION, Paris, France, Sept. 12-19, 1954. For information write: Colonel Julliard, Societe Internationale de Transfusion Sanguine, 53 Boulevard Diderot, Paris 12e, France.

INTERNATIONAL SOCIETY FOR CELL BIOLOGY, Leiden, Netherlands, Sept. 2-9, 1954. Professor Peter J. Gaillard, University of Leiden, Leiden, Netherlands, Secretary.

INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY, Washington, D. C., U. S. A., Sept. 6-10, 1954. Professor Fred C. Roulet, Hebelstrasse 24, Basle, Switzerland, Secretary-General.

JOURNEES MEDICALES, Paris, France, April 21-25, 1954. For information write: Secretariat of the Journees, 12, rue Pierre-Geofroix, Colombes (Seine) France.

LATIN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY, Caracas, Venezuela, Feb. 21-25, 1954. Dr. Victorino Marquez Reveron, Centro, Medico, Caracas, Venezuela, Secretary-General.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Medellin, Columbia, South America, Feb. 15-20, 1954. Dr. Cassius Lopez de Victoria, 176 East 71st St., New York 21, N. Y., U. S. A., Executive Director.

PAN AMERICAN CONGRESS OF OPHTHALMOLOGY (Interim), São Paulo, Brazil, June 17-21, 1954. Dr. Moacyr E. Alvaro, São Paulo, Brazil, President.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, Mexico, D.F., Mexico, Feb. 28-March 4, 1954. Dr. Pedro Hernandez Gonzalo, 8 No. 358, Vedado, Havana, Cuba, General Secretary.

PAN AMERICAN MEDICAL ASSOCIATION, International Medical Cruise Congress, S. S. Nieuw Amsterdam, Jan. 6-22, 1954. Dr. Joseph J. Eller, 745 Fifth Avenue, New York 22, N. Y., U. S. A., Executive Director.

PAN-PACIFIC SURGICAL CONGRESS, Honolulu, Hawaii, Oct. 7-18, 1954. Dr. F. J. Pinkerton, Suite 7, Young Bldg., Honolulu 13, Hawaii, Director General.

SECTIONAL MEETING, AMERICAN COLLEGE OF SURGEONS, London, England, May 17-19, 1954. Dr. Michael L. Mason, 40 East Erie St., Chicago 11, Ill., U. S. A., Secretary.

SOUTH AMERICAN CONGRESS OF ANGIOLOGY, Sao Paulo, Brazil, July 1954. For information write: Dr. Rubens Carlos Mayall, Rua Senador Vergueiro 73, Rio de Janeiro, Brazil, S. A.

WORLD CONGRESS OF CARDIOLOGY, Washington, D. C., and Bethesda, Md., U. S. A., Sept. 12-17, 1954. Dr. L. W. Gorham, 44 East 23d St., New York 10, N. Y., U. S. A., Secretary-General.

WORLD CONGRESS OF INTERNATIONAL SOCIETY FOR THE WELFARE OF CRIPPLES, Scheveningen-The Hague, Netherlands, Sept. 13-17, 1954. Secretariat: Miss H. P. Post, Pieter Lastmarkade 37, Amsterdam Z, Netherlands.

WORLD FEDERATION OF OCCUPATIONAL THERAPISTS, Edinburgh, Scotland, August 17, 1954.

WORLD MEDICAL ASSOCIATION, Rome, Italy, Sept. 26-Oct. 2, 1954. Dr. Louis H. Bauer, 345 East 46th St., New York 17, N. Y., U. S. A., Secretary-General.

DEATHS

Cary, Edward Henry ⊕ Dallas, Texas, President of the American Medical Association 1932-1933, died in the Medical Arts Hospital Dec. 11, aged 81. Dr. Cary was born in Union Springs, Ala., Feb. 28, 1872. His preparatory education was obtained at Union Springs Academy and high school in New York City, after which he entered Bellevue Hospital Medical College (New York University) and received the degree of doctor of medicine in 1898. After graduation he served an internship in Bellevue Hospital for one year, and an additional year as house physician at the New York Eye and Ear Infirmary. During the last year he was head of the ophthalmologic clinic of the Bellevue Hospital Medical College. He moved to Dallas in 1901, in 1902 became dean of the Dallas Medical School, and led in the movement to make it a department of Baylor University in 1904. He continued as dean of the Baylor University Medical School until 1929, when he became dean emeritus. From 1909 to 1929 he was chairman of the staff of Baylor University Hospital. During all this time, from 1902, Dr. Cary was professor and head of the department of ophthalmology and otolaryngology in both schools. He was instrumental in developing Baylor University Medical School into one of the leading institutions in the Southwest. In 1939, with a group of Dallas business men, he organized the Southwestern Medical Foundation, of which he was president of the board of trustees, and which on May 5, 1943, began the Southwestern Medical College, now known as Southwestern Medical School of the University of Texas, where he was professor emeritus of ophthalmology. He was presented with the 1945 award, given by Linz Brothers to the "outstanding citizen of Dallas." Dr. Cary was cited for his activities as a medical educator and principally for his work as founder and director of the Southwestern Medical Foundation. He organized the Baylor Medical Unit, which served in France in World War I. During World War II he was a member of the Appeal Board of Selective Service District No. 7. He was a Trustee of the American Medical Association from 1925 to 1929, became President-Elect in 1931, President 1932-1933, and was a member of its House of Delegates in 1906, 1909-1910, 1915-1916, from 1918 to 1923, in 1925, and from 1934 to 1951. For many years his annual contributions to the scientific exhibit at Association meetings were of distinct educational value. He was Chairman of the Committee on Legislation. Among the honors bestowed on Dr. Cary in his long and distinguished medical career have been the presidencies of the Dallas County, Texas State, Texas Ophthalmological and Otological, and Southern Medical associations. He was president of the executive board of the National Physicians Committee, the Philosophical Society of Texas, the Medical Arts Hospital, and the Group Hospital Service. A specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology, Dr. Cary was a member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, and the Association for Research in Ophthalmology, and fellow of the American College of Surgeons. He was a consultant in ophthalmology at Baylor University Hospital, Parkland Hospital, and the Medical Arts Hospital. In 1916 he received the degree of doctor of laws from Baylor University. Dr. Cary was a builder of medical buildings and institutions, a director of many corporations, and president of several others. His name was associated with the development and use of the Medical Arts Building in Dallas. Dr. Cary was head of Cary Clinic and contributed to the literature of ophthalmology.

EDWARD HENRY CARY, 1872-1953

Spalding, Edward D., ⊕ Detroit; born in Detroit Dec. 29, 1892; Johns Hopkins University School of Medicine, Baltimore, 1918; interned at Baltimore City Hospital and served a residency at New Haven (Conn.) General Hospital; professor of clinical medicine at Wayne University College of Medicine; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Detroit Academy of Medicine and the Detroit Medical Club; immediate past president of the Wayne County Medical Society and Michigan State Medical Society; Alternate Delegate to the American Medical Association; served overseas during World War I; during World War II served with the Harper Hospital unit as chief of medicine with duty in Casablanca, Oran, and Naples; later in the war attained the rank of colonel, and was medical consultant to the Fifth Army; attending physician and chief of division of cardiology, Harper Hospital; attending physician, City of Detroit Receiving Hospital; consultant in medicine, Veterans Administration Hospital in Dearborn and Charles Godwin Jennings Hospital; consultant in cardiology, Herman Kiefer Hospital; aged 60; was shot and killed Nov. 30, by a mental hospital escapee.

Woodyatt, Rollin Turner ⊕ Chicago; born in Chicago June 3, 1878; Rush Medical College, Chicago, 1902; appointed associate professor of medicine at his alma mater in 1912; later clinical professor at the University of Chicago, and chairman of the department of medicine at his alma mater; clinical professor of medicine emeritus (Rush) University of Illinois College of Medicine; specialist certified by the American Board of Internal Medicine; honorary president of the Chicago Diabetes Association; past president of the Association of American Physicians and the American Society for Clinical Investigation; member of the Central Society for Clinical Research, American Diabetes Association, the Endocrine Society, American Society of Biological Chemists, American Chemical Society, Sigma Xi, Sigma Chi, and Phi Rho Sigma; served during World War I; for many years on the staff of the Presbyterian Hospital; died in the Wesley Memorial Hospital Dec. 17, aged 74.

Milliken, Nathan Townley ⊕ Norwich, Vt.; born in Canandaigua, N. Y. May 4, 1906; Yale University School of Medicine, New Haven, 1932; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Phy-

⊕ Indicates Member of the American Medical Association.

sicians; assistant professor of medicine at Dartmouth Medical School in Hanover, N. H.; served during World War II; on the staff of the Hitchcock Clinic in Hanover, N. H.; consultant at the Veterans Administration Hospital in White River Junction, Vt.; affiliated with Mary Hitchcock Hospital in Hanover, N. H., where he died Aug. 9, aged 47, of carcinoma of the lung.

Abbott, Fred Edgerton ⊕ Oceanside, Calif.; Rush Medical College, Chicago, 1908; served during World War I; died in Santa Ana Sept. 24, aged 71, of coronary insufficiency.

Alderson, James, Strawberry Point, Iowa; Northwestern University Medical School, Chicago, 1891; formerly practiced in Dubuque, Iowa, where he was mayor, president of the board of education, member of the city council, and superintendent of the Finley Hospital; died Nov. 2, aged 89, of coronary occlusion.

Alleman, Frank ⊕ Lancaster, Pa.; Jefferson Medical College of Philadelphia, 1896; also a graduate in pharmacy; fellow of the American College of Surgeons; served as president of the board of health; past president of the Lancaster City and County Medical Society; an honorary member of the staff of Lancaster General Hospital, where he died Nov. 10, aged 82, of pulmonary embolus following operation for carcinoma of the kidney.

Collins, Burnett Charles, New York City; Long Island College Hospital, Brooklyn, 1894; fellow of the American College of Surgeons; served on the staffs of the Brooklyn Eye and Ear Hospital and the Swedish Hospital; died Nov. 17, aged 81, of heart failure.

Dalton, William Bart ⊕ Gordonsville, Tenn.; University of Louisville (Ky.) Medical Department, 1894; past president of the Smith County Medical Society; died in Nashville Nov. 1, aged 83, of cerebral thrombosis.

Emanuel, Max ⊕ Vineland, N. J.; Medizinische Akademie Düsseldorf, Düsseldorf, Germany, 1928; affiliated with Newcomb Hospital, where he died Oct. 31, aged 50, of cerebral occlusion.

Etz, Samuel Irving, New York City; Columbia University College of Physicians and Surgeons, New York, 1948; served during World War II; interned at the Boston City Hospital; assistant resident, department of obstetrics and gynecology at the New York Hospital; died Nov. 5, aged 28.

Finch, Henry C., ⊕ Anadarko, Okla.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1923; area medical officer, Bureau of Indian Affairs; served during World War II; died in Kansas City, Mo., recently, aged 54.

Fox, William Garfield ⊕ Lancaster, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; affiliated with Lancaster General Hospital, where he died Oct. 29, aged 74, of carcinoma of the lung.

Garnett, Alexander Yelverton Peyton ⊕ Washington, D. C.; University of Virginia Department of Medicine, Charlottesville, 1906; specialist certified by the American Board of Obstetrics and Gynecology; formerly associate professor of obstetrics at Georgetown University School of Medicine; affiliated with Garfield Memorial Hospital; died Nov. 4, aged 72, of coronary insufficiency.

Gessel, Udell Mathews ⊕ Los Angeles; Creighton University School of Medicine, Omaha, 1939; interned at Holy Cross Hospital in Salt Lake City; specialist certified by the American Board of Orthopaedic Surgery; served during World War II; affiliated with Orthopaedic and Los Angeles County General hospitals; died Oct. 23, aged 42.

Gilpatrick, Roy Hawkes ⊕ Cocoa, Fla.; Harvard Medical School, Boston, 1905; member of the Massachusetts Medical Society; formerly practiced in Nantucket, Mass., where he was on the staff of the Nantucket Cottage Hospital; died Oct. 11, aged 76.

Guest, John L., San Antonio, Texas; Barnes Medical College, St. Louis, 1901; died in Amarillo recently, aged 76, of cancer.

Harris, William Thomas ⊕ Troy, N. C.; Medical College of Virginia, Richmond, 1925; a trustee of the Greater University of North Carolina and a member of the board of directors of the Education Foundation; on the staff of Montgomery Memorial Hospital; died Oct. 21, aged 52, of coronary thrombosis.

Hursh, Robert McGuigan ⊕ Harrisburg, Pa.; Medico-Chirurgical College of Philadelphia, 1912; served during World War I; city health officer; died Nov. 13, aged 66.

Johnston, William ⊕ Boston; McGill University Faculty of Medicine, Montreal, Canada, 1897; died in the Boston City Hospital Oct. 15, aged 83, of cardiac asthma and rectal cancer.

King, Parks McCombs ⊕ Charlotte, N. C.; University and Bellevue Hospital Medical College, New York, 1902; first secretary and past president of the Mecklenburg County Medical Society; formerly on the faculty of North Carolina Medical College; died Oct. 11, aged 75, of acute coronary occlusion.

Lengby, Frederick Alexander, Minneapolis; University of Minnesota Medical School, Minneapolis, 1944; interned at Bethesda Hospital in St. Paul; served during World War II; died in Prescott, Wis., Sept. 18, aged 47.

Lewis, Edward James ⊕ Chicago; Rush Medical College, Chicago, 1907; formerly on the faculty of his alma mater; served on the staffs of Cook County and Michael Reese hospitals; died Nov. 25, aged 67, of coronary thrombosis and cerebral thrombosis.

Linder, Samuel, Brooklyn; Cornell University Medical College, New York, 1910; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; on the staffs of the Crown Heights and Jewish hospitals; died Nov. 17, aged 67, of acute coronary occlusion.

Loizeau, Charles Edward ⊕ Dubuque, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1904; served actively for many years as an officer of the Northeast Iowa Area, Boy Scouts of America, and received the first Beaver award presented in the four county area; died in Mercy Hospital Oct. 23, aged 78, of left ventricular failure.

Miles, Charles Gardner ⊕ Brockton, Mass.; College of Physicians and Surgeons, Baltimore, 1908; past president of the Plymouth District Medical Society; served on the school committee and as city physician; died Oct. 3, aged 73, of coronary thrombosis and rheumatic heart disease.

Miller, Edward Alexander ⊕ Sagamore Beach, Mass.; Boston University School of Medicine, 1899; died Oct. 14, aged 81.

O'Neal, Orvil ⊕ Ripon, Wis.; St. Louis University School of Medicine, 1910; president of the medical staff of Ripon Municipal Hospital; died in Madison Nov. 24, aged 70, of duodenal obstruction and carcinoma of the pancreas.

Ostheimer, Maurice, Whitford, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; formerly assistant professor of pediatrics at his alma mater; served as secretary of the state milk commission and as chief diagnostician for the city board of health; died Oct. 28, aged 80.

Skillman, Wilbur Francis ⊕ Baltimore; University of Maryland School of Medicine, Baltimore, 1900; affiliated with Lutheran and Union Memorial hospitals; medical director at Masonic Home at Cockeysville; died Nov. 6, aged 75, of abdominal malignancy.

Wenrich, George Gockley ⊕ Wernersville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1894; an Associate Fellow of the American Medical Association; served as a member of the board of health and treasurer of the school board; formerly director of the Wernersville National Bank; died Oct. 29, aged 82, of arteriosclerosis.

Wertz, Harry W., Montpelier, Ohio; Kentucky School of Medicine, Louisville, 1890; for many years county health officer; an officer in the Medical Corps, U. S. Army, during World War I; served as county coroner, a member of the Williams County Board of Health, and at Montpelier as a member of the boards of education and of public affairs and as village health officer; district surgeon for the Wabash Railroad; died Nov. 12, aged 84, of heart block.

Whitman, Clayborne Russell, Tuscumbia, Ala.; Birmingham Medical College, 1909; high school football physician and surgeon for the Southern Railway; affiliated with Colbert County Hospital in Sheffield; died Oct. 30, aged 70, of coronary occlusion.

GOVERNMENT SERVICES

ARMY

Korean Officers to Study at Brooke Hospital.—Six officers of the Republic of Korea Medical Corps have arrived at Brooke Army Medical Center, Fort Sam Houston, Texas, to spend six months observing medical and surgical techniques. Colonels Kim Hak Hyun and Oh Hi Su, who commanded the R. O. K. 5th and 15th Army hospitals, respectively, will observe methods of orthopedic surgery practiced at the hospital. Internal medicine will command the attention of Colonels Kim Nan Nym and Son Yong Su, who formerly headed the R. O. K. 3rd and 18th Army hospitals. The remaining two officers, Col. Kim Yong Eun and Lieut. Col. Lee Kyung Nak, will concentrate on general surgical methods at the hospital. Colonel Kim's last assignment was as deputy commandant of the R. O. K. Medical Field Service School, while Colonel Lee was formerly chief of professional services in the Office of the R. O. K. Surgeon General.

Certificates of Appreciation for Malaria Research.—At a ceremony in the Army Surgeon General's Office, Washington, D. C., Nov. 20, certificates of appreciation were awarded to Dr. Alf S. Alving, professor of medicine, University of Chicago, G. Robert Coatney, Ph.D., of the laboratory of tropical diseases, National Microbiological Institute, U. S. Public Health Service, and Dr. Ralph Jones Jr., assistant professor of research medicine, University of Pennsylvania School of Medicine, Philadelphia, for their research in connection with the development and testing of primaquine, an antimalarial drug. Dr. Alving worked with the wartime committee on medical research of the Office of Scientific Research and Development and later with the U. S. Public Health Service, and since 1950 directly with the Army's medical research and development program. He arranged and maintained a research facility in Stateville Prison at Joliet, Ill., where medical officers worked under his direction in studying a vast array of antimalaria drugs under controlled conditions. He also supervised tests on the toxicity of primaquine on volunteers at Fort Knox, Ky., and on more than 3,000 troops returning from Korea.

Dr. Coatney was awarded the certificate for outstanding patriotic civilian service to the Army from January, 1951, to June, 1953, when "he was in charge of malaria chemotherapy studies undertaken by the Surgeon General to explore the curative effectiveness of several 8-aminoquinolines in prisoner volunteers at Atlanta, Ga., and in Korean returnees at Fort Benning, and of other tests initiated to determine the antimalarial properties of daraprim," another antimalarial drug. Dr. Jones was awarded the certificate for outstanding patriotic civilian service to the Army from June, 1951, to April, 1953, when "he was responsible for supervising the clinical testing of primaquine as a curative drug for Korean vivax malaria in Army hospitals at Fort Knox, Fort Meade, Camp Breckinridge, Fort Dix, and in the Naval Hospital at the Marine Base at Camp LeJeune."

DEPARTMENT OF DEFENSE

Society of Medical Consultants.—The Society of Medical Consultants to the Armed Forces held its eighth annual meeting at Walter Reed Army Medical Center, Washington, D. C., Nov. 23. Dr. John Minor, chief of medical service at Emergency Hospital, Washington, D. C., president of the society, spoke of the problems confronting consultants to the military services. Other speakers were Gen. Matthew B. Ridgeway, U. S. Army Chief of Staff; Major Gen. George E. Armstrong, Surgeon General of the Army; Rear Adm. Clarence J. Brown (MC), U. S. N., assistant chief of the Bureau of Medicine and Surgery; Col. Oscar S. Reeder (MC), U.S.A.F., deputy director of professional services, Office of the Surgeon General; Dr. Stanhope Bayne-Jones, technical director of research, Office of the Army Surgeon General; and Col. Joseph R. Shaeffer (MC), chief surgical consultant, Office of the Army Surgeon General. At the evening dinner, which was held at the officers' mess, the speaker was Major Gen. Guy B. Denit (MC), retired.

VETERANS ADMINISTRATION

Residencies in Neurology Available at San Francisco.—Residencies in medical neurology are available at the U. S. VA Hospital, San Francisco, beginning July 1, 1954. The residency program is under the direction of the Combined Stanford University Medical School and University of California School of Medicine Deans' Committee. The training is fully accredited by the American Board of Psychiatry and Neurology for a period of two years.

MISCELLANEOUS

Psychiatric Interns and Residents Wanted.—The U. S. Civil Service Commission has announced a new medical officer examination for filling the positions of rotating intern, $2,800 a year, and resident in training in psychiatry and in neurology, $3,400 to $4,200 a year, in St. Elizabeths Hospital in Washington, D. C. Appointments are to begin on July 1, 1954. This hospital is a federal psychiatric hospital with about 7,000 patients.

Appropriate education is required, plus, for the resident positions, successful completion of a full year's internship. No written test is required. Applicants must not have passed their 35th birthday (waived for persons entitled to veteran preference). Applications will be accepted by the Executive Secretary, Board of U. S. Civil Service Examiners, St. Elizabeths Hospital, Washington 20, D. C.

Positions Open in Food and Drug Administration.—The Food and Drug Administration of the U. S. Department of Health, Education, and Welfare is actively recruiting medical officers to work in Washington, D. C. The positions pay an entrance salary of $7,040 to $9,600 with increments. The duties of the positions provide for medical decisions relating to food, drugs, devices, and cosmetics, as well as participation in the medical phases of legal actions against violative products. For further information write to Dr. Irvin Kerlan, Acting Medical Director, Food and Drug Administration, Washington 25, D. C. Interested physicians should also file for Medical Officer Examination, Examining Circular EC-24, issued April 5, 1950, with the U. S. Civil Service Commission, Washington 25, D. C., stating special preference for a position with the Food and Drug Administration.

Psychiatrists and Psychologists Needed.—The U. S. Attorney General has instructed the director of the Federal Bureau of Prisons to implement the Youth Corrections Act as provided by Public Law 865, 81st Congress (Section 5005-5024). The federal correctional institution at Ashland, Ky., probably will be designated as the first diagnostic and treatment center for these youthful offenders. It started receiving commitments Dec. 1, 1953, under the Youth Corrections Act. Other centers will be designated as the law is utilized by federal judges. Psychiatrists and psychologists with special training or particular interest in intensive study and treatment of youthful offenders are needed. Psychiatrists and psychologists with Ph.D. degrees will be employed as commissioned officers of the U. S. Public Health Service; psychologists who have special qualifications but who have not obtained Ph.D. degrees will be employed under the Civil Service Commission. Persons who accept a commission with the U. S. Public Health Service can thereby fulfill Selective Service obligations. Those interested should correspond with the Medical Director, Bureau of Prisons, Washington 25, D. C., or the Division of Commissioned Officers, U. S. Public Health Service, Washington 25, D. C.

FOREIGN LETTERS

DENMARK

Centralization of Treatment of Tetanus.—Recent correspondence in the Danish medical press suggests that the treatment of tetanus would be more effective if patients with this disease could be centralized in hospitals provided with a specially trained staff and special facilities. Isolated reports, each of only a few cases, show that in some hands barbiturates and various anesthetics are effective, while other reports reflect the modern tendency to give curare to ensure relaxation of muscles without inducing respiratory paralysis. Scarcely 50 cases of tetanus are reported in Denmark every year, and the principle of centralized treatment already applied to narcotic poisoning and poliomyelitis would be advantageous in the treatment of this disease because the prognosis depends largely on the highly technical skill with which it is treated. Acidosis, dehydration, anuria, and shock are among the many factors that may decrease the chance for survival, and it is only the well-equipped hospital with special provision for artificial ventilation of the lungs and other measures that can meet every call on it satisfactorily.

A small number of patients with tetanus (93 in 12 years) have been treated at the Blegdam Hospital, which has lately acquired an international reputation for pioneer work in the treatment of poliomyelitis. Twenty-eight of the 93 patients died. With the successful use of positive pressure ventilation in treating poliomyelitis in mind, this treatment has lately been used in tetanus. Three members of the staff of this hospital, Drs. B. Björneboe, Björn Ibsen, and Steen Johnsen, have recently reported the case of a 10-year-old boy whose recovery from tetanus may well be traced to the excellent treatment he received. Conditions hitherto regarded as hopeless can now be cured when curare is combined with tracheotomy, positive pressure ventilation, antibiotics, restoration of the fluid balance, and other devices for preventing and combating shock. Such skillful combined treatment is not available in many small hospitals.

Treatment of Cerebral Apoplexy.—Danish vital statistics rank cerebral apoplexy as the third commonest cause of death following only heart disease and cancer. According to some statistics, 70 to 80% of all patients with apoplexy died soon after the onset. At least two large Danish hospitals recognize the importance of a neurological examination in the diagnosis and treatment of apoplexy and admit these patients directly to the neurological department. This rule has been applied for several years in the Frederiksberg Hospital from which a recent report is published in *Ugeskrift for Laeger* for Oct. 15, 1953, by Dr. T. Dalsgaard-Nielsen. The report deals with about 1,300 patients treated in the period from 1940 to 1952. On admission to the neurological department of this hospital, the blood pressure, hemoglobin, blood sugar, and blood urea levels, Wassermann reaction, temperature, pulse, respiration, and urinalysis of every patient are recorded. This study shows a mortality lower than that hitherto associated with this condition. To prevent phlebitis, hypostatic pneumonia, and bed sores, the patients were allowed out of bed as soon as possible, and passive movements with massage were started on the first day. Soon afterward, active movements and occupational therapy were encouraged, and the patient was taught to walk with the support of another person or a cane. To avoid collateral edema of the brain, dehydration was encouraged by giving magnesium sulfate by the mouth and, in many cases, an intravenous injection of 50 ml. of a 50% solution of dextrose. Morphine, scopolamine, and large doses of other sedatives were consistently avoided, and in no case was surgery attempted. It was hoped that modern refinements of diagnostic tests would facilitate the differential diagnosis of cerebral hemorrhage, thrombosis, and embolism, but in many cases it was not possible to draw the line clearly between these conditions. It is pointed out in a leading article in the same issue that the former rules with regard to the differential diagnosis are no longer valid. We can no longer trust implicitly in the old teaching that the apoplectic patient who is unconscious must be suffering from a hemorrhage or that this diagnosis must be dismissed if the cerebrospinal fluid is clear.

Cancer Conference in Copenhagen.—In the autumn of 1953, the Danish National Association for Combating Cancer celebrated its 25th anniversary by holding an inter-Scandinavian conference. The occasion was marked by a special number of *Ugeskrift for Laeger* that contained among other things a statistical study of cancer of the lungs, with special reference to its possible connection with smoking. Professor Berven of Sweden noted that 25% of the patients with lung cancer in the Swedish records were not smokers. Dr. Pedersen of Norway expressed doubt of a real increase of the incidence of lung cancer in his country.

LONDON

Address on Orthopedics.—"An Even Keel in Orthopaedics" was the title of Mr. H. Jackson Burrows' presidential address to the section of orthopedics of the Royal Society of Medicine, which has just been published in the proceedings of the society (*Proc. Roy. Soc. Med.* **46:**805, 1953). He said in part: "More than half the boys leaving public schools have lost their tonsils, and as many as four in five their foreskins. One wonders how many have been subjected to wedged shoes and so-called remedial exercises: certainly a very large number, and I am persuaded that it is scarcely possible to be a really nice young man without having endured these indignities of initiation. Normal children go through a phase of knock-knee, which soon disappears if they are lucky enough to avoid treatment; if, on the other hand, they have to contend with a man-made pes varus, they usually still get well, but much more slowly. I am not speaking of that textbook extravagance, the quarter-inch wedge; it is impossible; its victims never return, and so it continues to be sponsored. 'Remedial exercises' are a worse expedient than wedges, because more time-consuming, more expensive and more harmful. In one girls' school, five in every seven pupils perform daily the rite of 'flatters,' described in the school bill as remedial exercises. . . . When I was a child our nannies (beloved but now extinct race) made us turn our toes out; nowadays our physiotherapists would make us walk on the outer sides of our feet; far better nanny's valgus than physio's varus.

"In an age when cleverness is often prized above wisdom and integrity, the paramount importance of the patient's interests cannot be stressed too strongly. Some surgeons have found in the intervertebral disc not a jelly-like nucleus pulposus but a glittering nugget of gold: a great surgical advance has been discredited by misuse. . . . The development of arthroplasty of the hip is another great advance of our time, and a lasting memorial to Smith-Petersen, but it remains a truism that a surgeon makes provision for his later years by 'doing some cups' in his youth. A stern task confronts those who will have to deal with the failures of the Judet operator, so recent an operation as to be rarely proper in any but the aged. In our youth most of us have designed gadgets, and in our maturity have regretted them.

"How often has the pursuit of 'orthopaedic principles' converted a person who could sit but not stand into one who could stand but not sit? The supreme example is provided by the orthopaedic epitaph 'He died in perfect position.' I knew a natural exhibitionist with flail legs, who earned a reasonably happy competence by walking about race courses and football fields on his hands with his feet tucked into his waistcoat

The items in these letters are contributed by regular correspondents in the various foreign countries.

pockets. Someone fused one knee and the patient was ruined. Later the other knee was fused, equally unwisely, and ultimately his legs were cut off through the thighs. In poliomyelitis an ill-judged lengthening of the tendoachillis notoriously can impose a caliper for life, but in spastic paralysis it can cause the most devastating multiple deformities. Bone operations on growing feet provide a more controversial subject. I believe them to be rarely excusable. When I was a registrar at the Royal National Orthopaedic Hospital I saw a master perform many arthrodeses most beautifully on young children's feet. Later, I inherited these patients and have seen the deplorable results, irredeemable by further surgery. Among [these] badly disabled children . . . such feet present some of our worst problems—feet that have been ruined less by the hand of disease than by the hand of man."

Quality in General Practice.—One of the paradoxes of the British National Health Service is discussed in an annotation in the *British Medical Journal* of Oct. 3. Although it might be thought that postgraduate training in clinical medicine would make a man preeminently suited to general practice, the difficulties experienced by many holders of higher qualifications, and especially the membership of the Royal College of Physicians, in entering general practice suggest that there are at least some established physicians who do not share this view. Many practitioners believe that a physician, however well qualified in medicine, must begin at the beginning when he starts in general practice and not expect to become immediately a principal in a large practice ready-made for him. Nor, indeed, is he likely to get far, if he enters general practice with an air of doing so as a last resort and with an expectation of obtaining part-time hospital work soon. Those responsible for his appointment to a vacancy, whether as assistant or principal, may well take care to assure themselves that he intends to devote his whole energy to general practice. But when allowance is made for those few registrars who take no heed of such criteria as these, there remain many applicants who believe that they have been turned down for no other reason than that they have done several years of postgraduate work in hospitals and achieved a higher qualification. There is more than a grain of truth in the jocular remark, which came from a good source, that "to the applicant for a general-practice vacancy the possession of a car is more important than the possession of a Membership of the Royal College of Obstetricians and Gynaecologists, the Fellowship of the Royal College of Surgeons, or—most dangerous encumbrance—membership of the Royal College of Physicians."

Although general practice is a special branch of medicine, its greater part is still clinical medicine. It may gather tributaries from other springs of knowledge, but a thorough foundation in general medicine can be nothing but an asset.

Mothers in Industry.—The effect on home life and child welfare of the increasing extent to which married women are seeking employment has caused concern in recent years, and a joint committee of the Medical Research Council and the Department of Scientific Research is investigating as a matter of urgency the role of mothers in industry. The views of the British Council of Churches have been summarized as follows: "(1) . . . married women will continue to be employed in industry and . . ., apart from the economic factor, many find satisfaction in such employment. In the case of mothers, however, the true interests of the child should have a prior claim over the other considerations. (2) This will normally mean that the mother who has the care of children not yet at school should not seek employment outside the home. (3) When the children are at school a number of considerations have to be weighed before the mother makes her decision. (4) If she decides to seek employment in industry, employers for their part should give more consideration to the possibilities of part-time work and more flexible hours of employment."

At the same time a deputation, representing various interested nursing organizations, including the Royal College of Nursing, has met with the Minister of Health. They stated that the provision for children in day nurseries and nursery schools was inadequate, and that a working party should be set up to consider the day-time care of children under 5. What is worrying a lot of persons, including physicians, is the extent to which the authority and responsibilities of parents are being shelved. What is the effect going to be on the rising generation if mothers, as well as fathers, go out to work every day, leaving their children in the care of day nurseries and nursery schools? Is the day coming when we shall have a Ministry of Child Culture that will organize national day nurseries all over the country into which infants will be placed the moment they are born, leaving the parents with no responsibility whatsoever for their future development? If family life is the basis of Western civilization, then the mother's place is at home at least as long as there are children of preschool or school age.

Accidental Poisoning in Childhood.—An analysis of 502 cases of accidental poisoning in children under the age of 12 years, seen at the Royal Hospital for Sick Children, Edinburgh, and the Royal Aberdeen Hospital for Sick Children in the years 1931-1951, has just been published (Craig, J. O., and Fraser, M. S.: *Arch. Dis. Child.* **28**:259, 1953). A tenfold increase in such cases occurred between 1931 and 1951; in 1931 there were 5 cases annually and in 1951 there were more than 50. The causative agents are classified as follows: group 1, household substances, e. g., disinfectants, fuels, cleaning agents, and insecticides, 203; group 2, medicines, including those intended for internal use, e. g., camphor, barbiturates, iron, and salicylates, 185, and those intended for external use, e. g., liniments and nose and eye drops, 75; group 3, vegetable matter, e. g., seeds and berries, 35; and group 4, source unidentified, 4.

Throughout the period covered by the investigation there was a steady increase in the number of cases due to household substances, but after 1948 there was a sudden sharp rise in the number due to medicines. More than half the cases (331) occurred between the ages of 1 and 3 years, and only 38 after the age of 5. About three boys were poisoned for every two girls.

The sharp rise in medicinal poisoning in 1948 is attributed to the increased prescribing under the National Health Service. It is pointed out that "many of the 'new' prescriptions have gone to homes where overcrowding and lack of experience in dealing with medicines might cause them to be poorly guarded."

Duke of Edinburgh in Royal College.—Another member of the Royal Family has honored the Royal College of Surgeons by accepting the honorary fellowship of the college. This is the Duke of Edinburgh, who visited the college on Oct. 20 to receive the diploma of fellowship. In his acceptance speech he took up a point made by the president of the college in his speech of welcome to the effect that surgery was both an art and a science. As a mere layman, he (the Duke) hoped that the practitioner artist and the scientific researcher would always continue to work in close harmony. He also expressed satisfaction in becoming an honorary surgeon, because he felt that, if ever he came under the surgeon's knife, the surgeon would remember that he was operating on a colleague.

Tablet to the Memory of John Radcliffe.—The unveiling of a stone tablet to the memory of John Radcliffe in the University Church of St. Mary, Oxford, on Oct. 17, was described as "an act of reparation to the memory of a great benefactor of the University." John Radcliffe, one of the best known physicians at the turn of the 17th century, attended several members of the Royal Family. In one of his more caustic moments Osler described him as the man who was "remembered, first by the Gold-headed Cane, second by never having written a line, and third by the superb monuments which exist to his memory." He was a graduate of Oxford and his will made large bequests to the university, where his name is perpetuated in the Radcliffe Infirmary, the Radcliffe Observatory, and Radcliffe Travelling Fellowships. He died in November, 1714, and was buried in St. Mary's Church. For many years the exact location of his grave was not known. About 1820, however, on opening a grave near the supposed spot, a gold coffin-plate was found that bore the simple inscription: John Radcliffe, M.D., died November 1, 1714, in the 65th year of his age. This was copied and engraved on the stone floor immediately over his place of burial. Everyone was under the impression that adequate honor had been done him until quite

recently. Dr. C. R. Hone, a former Bishop of Wakefield where Radcliffe was born, discovered that Radcliffe had expressed the wish that a tablet should be erected to his memory in the church. This wish was not fulfilled immediately and eventually was forgotten. It was in fulfillment of this almost 250-year-old wish that the memorial stone has now been unveiled and dedicated.

Royal Commission on Mental Illness.—The Prime Minister has just announced in Parliament that a Royal Commission is to be set up "to inquire as regards England and Wales into the existing law and administrative machinery governing the certification, detention, care (other than hospital care or treatment under the National Health Service Acts, 1946-52), absence on trial or license, discharge and supervision of persons who are, or are alleged to be, suffering from mental illness or mental defect; . . . to consider as regards England and Wales the extent to which it is now, or should be made, statutorily possible for such persons to be treated, as voluntary patients, without certification; and to make recommendations."

TURKEY

New Law Pertaining to Illicit Traffic in Narcotics.—Before World War I drug addiction was rarely encountered in Turkey. With the influx of Russian refugees in 1919, addiction, mostly to cocaine, appeared and spread. During the occupation, 1918 to 1923, it was difficult to curb illicit traffic in narcotics, and it became necessary to set aside a pavilion for the treatment of drug addicts at the Istanbul Bakirköy mental hospital. In recent years, drug addiction has greatly increased. From 1940 to 1949, 1,543 patients were treated for drug addiction at this hospital. In 1947, about 5,000 persons were using drugs or narcotics; it is estimated that there are from 25,000 to 30,000 doing so today. The extent of drug addiction among school children has not been ascertained.

The amendment of the drugs and narcotics law that came into effect this September provides that persons who violate the regulations pertaining to the legal production of narcotics or who engage in illicit production or illicit import or export, or who attempt to do so will be sentenced to not less than 10 years of hard labor and from 3 to 5 years of exile (under police supervision) after expiration of the term and a fine of 10 Turkish pounds for each gram of drug; the fine is to be not less than 1,000 pounds. If the drugs concerned are heroin, cocaine, morphine, or hashish, the offender is sentenced to hard labor for life. A person attempting to form an organization for the purpose of perpetrating any of the above-mentioned crimes and his associates will be sentenced to five years of hard labor; more than two persons are considered an organization. In the event of an established organization and active participation and if heroin, cocaine, morphine, or hashish are concerned, the death sentence is to be pronounced. For persons, and those acting as intermediaries, guilty of selling drugs to minors or persons not responsible for their actions, the penalty for the leader is raised by one-sixth and if narcotics are concerned the death sentence is given. For second or habitual offenders the penalty is raised by one-half, and if narcotics are concerned the death sentence is pronounced. All property of convicted persons is confiscated. Persons who, within the country, violate the regulations of the legal production and sale of drugs and narcotics or engage in their illicit production, buy, conceal, or transfer such goods, facilitate the use of narcotics by supplying quarters or otherwise assist in furthering the use of narcotics, or act as intermediaries will be sentenced to not less than five years of hard labor, from two to five years of police supervision in banishment after expiration of the prison term, and a fine of 10 pounds for each gram of drug; the fine is not to be less than 500 pounds. If the drugs concerned are heroin, cocaine, morphine, or hashish the offenders will be sentenced to 10 years of hard labor and a fine not less than 1,000 pounds and not less than three years banishment. Persons sheltering drug addicts are to be sentenced to from three to five years in prison and a fine of from 100 to 1,000 pounds. Second offenders will receive, in addition, a banishment sentence of not less than one year. By court decision and on the recommendation of a physician, drug addicts are sent to a hospital for treatment and kept there until recovery, after which they may be kept under police supervision for from 6 to 12 months. Persons who have participated in the above-mentioned crimes, but give information before that information is otherwise available to the police will have their sentence reduced. If the informers assistance leads to the arrest and conviction of their accomplices, the death sentence of an informer may be converted to hard labor for 15 years, a sentence of hard labor for life to not less than 10 years of hard labor; other sentences will be reduced by one-half.

If physicians, chemists, pharmacists, dentists, proprietors, or directors of laboratories or concerns manufacturing pharmaceuticals, veterinarians, civilian or military sanitary inspectors, trained or practical nurses, or midwives are guilty of the above-mentioned crimes, a sentence to hard labor for life shall be converted to a death sentence; if a temporary sentence to hard labor is pronounced, the sentence and the period of banishment is raised from one-third to one-half. The convicted persons will be ineligible for civil service and will have his license revoked for life. For persons who, because of the above-mentioned crimes, have caused a person to become a drug addict, to become ill, or to suffer injury, a sentence other than a death sentence or hard labor for life shall be raised one-third to one-half. If drug addiction has been occasioned in more than one person, the sentence is doubled, and, if a person died because of the addiction, illness, or injury, the death sentence will be pronounced.

Huntington's Chorea.—In *Dirim*, an Istanbul medical periodical, volume 28, number 8, Dr. Shükrü Hazim Tiner, chief of Istanbul Haseki Municipal Hospital, and his associate Dr. Ö. S. Dürüshken, reported a case of Huntington's chorea, which is rather rare in Turkey. Observation of involuntary movements of the 34-year-old man began five years ago when these movements did not interfere with the patient's work. They gradually increased until he could no longer work. Three years ago, the patient became irritable and easily excited. Fibrillary twitching at the mouth and convulsive movements of the feet appeared, but he was still able to walk. His childhood development was normal. He had not had any serious illness. He is married, had seven healthy children, and had never had gonorrhea or syphilis. His mother had undergone treatment for chronic chorea that was complicated by symptoms of mental disease and had died of Huntington's chorea. The mother's two sisters and the patient's two brothers also died of that disease. In the mother, the disease began at the age of 36, in the brothers between the age of 35 and 40. In the daughter of the maternal aunt, slight symptoms of the disease appeared at the age of 36. There is no history of oligophrenia, epilepsy, or other hereditary disease in this family that had seven members with Huntington's chorea in two generations. According to the patient, there was no such disease in his grandparents. In the patient's children and those of his brothers, there are as yet no symptoms of the disease.

Fifth International Congress of Tropical Medicine and Malaria.—The congress was held in Istanbul at the Shale Kiosk of the Yildiz Palace, the residence of the late Sultan Abdulhamid II, from Aug. 28 to Sept. 4 under the auspices of Celal Bayar, president of Turkey, and with Adnan Menderes, the Prime Minister, as honorary president. It was attended by 560 foreign delegates and their wives. Forty-two countries were represented. Prof. Ekrem Hayri Üstündag, the Minister of Health and Social Assistance, Prof. Fahreddin Kerim Gökay, the governor of Istanbul, diplomatic representatives, and the press attended. In his opening address, Prof. Üstündag gave a brief survey of malaria, once the chief public health problem in Turkey, which after 25 years of systematic antimalaria work and DDT spraying through the Marshall plan has finally come under control. There are no deaths now from malaria, and the index in malarial regions has dropped from 30.5 to 1.4%. Cholera and plague have not occurred for years. Enforcement of the vaccination law and border control have prevented outbreaks of smallpox. Campaigns against undulant fever, typhoid and typhus, trachoma and leprosy continue.

CORRESPONDENCE

SERPENTS' SENSE OF HEARING

To the Editor:—Now that processed snake venom, especially the neurotoxin of the cobra, is a recognized medicinal agent the following contribution to herpetological physiology and medical history may be of interest to physicians as well as to the general reader.

Snake charming is an art that has been practiced from very ancient times in Africa and the East. It often remains from generation to generation the profession of certain families. It is sometimes practiced for alleged useful purposes, for example, to clear a house of unwelcome snake visitors. For the most part, however, it is employed as a form of popular amusement in India and other countries. The frequent use of a musical pipe or fife and the way in which certain snakes, especially the cobra, seem to respond to the sounds are facts of interest to naturalists, in spite of the claims of some authorities that snakes are deaf. The chief species of snake susceptible to charming is the cobra, namely, the Indian hooded cobra or Naja naja tripudians and the Egyptian cobra or Naja haje. Serpents of all kinds are mentioned in the Hebrew scriptures under various names. Those who are interested in the subject might refer to a paper published in the *Bulletin of the History of Medicine* (15:359 [April] 1944).

There is no doubt at all from the empirical point of view that charming has been practiced very successfully, especially on cobras, from the most ancient times. The most famous reference to such snake charming is in Psalm 58, verse 5.

> Their poison is like the poison of a serpent:
> They are like the deaf adder that stoppeth her ear;
> Which will not hearken to the voice of charmers,
> Charming never so wisely.

This remarkable asseveration is especially appropriate at the present time when such wicked creatures, not deserving the name of human beings, perpetrate the most vicious and revolting crimes, as kidnapping children and cruelly murdering them in spite of entreaties and prayers of parents and offers of generous ransoms. How appropriate the psalmist's expression that these serpents deliberately stop up their ears and turn a deaf ear to avoid being "charmed" and softening their hearts! Another biblical reference to snake charming is in Jeremiah 8, 17:

> For, behold, I will shed serpents' basilisks among you
> Which will not be charmed.

Still another is in the Book of Ecclesiastes 10, 2:

> If the serpent bite before it is charmed,
> Then the charmer hath no advantage.

There is also a reference to charm in the Apocryphal Book of Ecclesiasticus 12, 13. It is well to note that the above verse 5 in Psalm 58 implies conversely that snakes and especially cobras, which are employed for the most part by snake charmers, do respond to sounds and are not ordinarily deaf—this in spite of the assertion by some zoologists that snakes anatomically speaking do not possess a highly developed sense of hearing. They suggest that the charming is done by "vibrations," but physiologically are not all sounds vibration waves?

In Shakespeare there are three references to the popular belief of deafness among serpents. One is in King Henry VI, part 2, act 3, scene 2, lines 76 and 77.

> What, art thou, like the adder, waxen deaf?
> Be poisonous too, and kill thy forlorn queen.

Another passage is found in Troilus and Cressida, act 2, scene 2, lines 168 through 173:

> The reasons you allege do more conduce
> To the hot passion of distemper'd blood
> Than to make up a free determination
> 'Twixt right and wrong; for pleasure and revenge
> Have ears more deaf than adders to the voice
> Of any true decision.

Finally, there is another line in Sonnet 112, lines 9 through 11:

> In so profound abysm I throw all care
> Of others' voices, that my adder's sense
> To critic and to flatterer stopped are.

The question as to the acuity of serpents' hearing is of timely interest in connection with an incident that occurred recently in Springfield, Mo., where a number of cobras were let loose or escaped from the premises of a snake dealer and keeper. Some of these were recaptured, but others were not caught. A novel stratagem was then thought of. A phonograph record of a snake charmer's "music" or cacophony was obtained from India and played on a phonograph with a loud speaker in Springfield. According to the news dispatches, this lured out the missing hooded cobra, which, according to witnesses, responded to the sounds (*St. Louis Post-Dispatch*, 1953). This report of an authenic episode speaks strongly in favor of a well-developed sense of hearing in the cobra; contrary to assertions of some skeptics, that the "charming" of snakes is not done by sounds but by the gesticulations of the charmer.

In order to conclude the argument in favor of a well-developed sense of hearing in cobras, I interviewed five well-educated Hindu physicians from different parts of India. These scientists were doing graduate work at the Sinai Hospital in Baltimore. Each one of these physicians expressed his firm conviction that the charming of cobras is a well-known empirical and established fact and that there was no doubt that these serpents responded to certain musical tones. Furthermore, I was told that certain forms of music practiced by the charmers excited the reptiles more than other forms. Finally, I learned that it was a common practice among natives of India to caution children, when out playing in the dark in the countryside, that they should not sing lest their sounds attract the dangerous reptiles. Thus, it seems that, as between Shakespeare and the scriptures, the former was merely repeating a popular misconception and superstition about deafness of snakes, whereas, the psalmist employed a metaphor from natural history, which, as in so many other passages of the scriptures, was absolutely correct both literally and figuratively.

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SURGICAL HYPOTHERMIA

To the Editor:—There is need to correct inaccuracies in the recent literature on surgical hypothermia. Lewis (*Surgery* 33:52, 1953) refers first to Fay and "a little later, regional refrigeration." My work (*Tr. A. Am. Physicians* 52:189, 1937; *Surg., Gynec. & Obst.* 67:746, 1938; *Surgery* 3:893, 1938; *Arch. Surg.* 38:155 [Jan.] 1939) antedated Fay experimentally and clinically, though the two lines of work were separate and independent. Lewis continued that regional refrigeration "seems no longer to be of interest. Other anesthetic agents are better." This statement is true to the extent that local refrigeration has been largely abandoned, unjustifiably, and mostly by surgeons who find refrigeration inconvenient because they have not acquired the technique. Skilled anesthesia of other kinds may sometimes not aggravate shock, but refrigeration is the sole method that can prevent shock. Lewis accepts the benefits of systemic hypothermia while ignoring the shock still produced unnecessarily by surgeons who perform severe limb operations without hypothermia.

Fay's valuable work was largely neglected. Others besides myself have supported his original suggestion of reduced body

temperature in shock treatment, but the harmful tradition of warming shocked patients still largely prevails. He did not propose hypothermia for prevention of shock during operations. I adopted Fay's method for this purpose experimentally. Lacking such surgical collaboration as Crossman had furnished for local refrigeration, my paper had to be limited to animal experiments without clinical trials. But this paper (*Anesth. & Analg.* **29**:97, 1950) gave the essential facts of hypothermic reduction of shock and of the need for anesthetics and the lengthened time for which anoxia can be tolerated. The reduced blood pressure that operators seek to attain with more or less risky drugs is produced automatically and safely by low temperature. The weakness or dangers from Fay's prolongation of "hibernation" for several days do not arise from a few hours of radical cooling, which is remarkably well borne. I pointed out precisely the operations for which this method should serve, including some for which surgeons have not yet utilized it. It should be routine for all extremely long operations on children, including the surgical separation of Siamese twins. This priority in laying down the basic principles of hypothermic surgery has remained unmentioned by all subsequent writers, including the most recent (*J. A. M. A.*, **153**:1081 [Nov. 21] 1953).

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CORTISONE AND THROMBOEMBOLISM IN SHOULDER-HAND SYNDROME

To the Editor:—In a recent report in THE JOURNAL (**153**:788 [Oct. 31] 1953), Steinbrocker and associates recorded their extensive experience in the management of the shoulder-hand syndrome and presented a challenging comparison between sympathetic block and corticotropin and/or cortisone therapy. Although these authors found that steroid administration gave almost as good results as stellate block, they regard the latter as the treatment of choice for shoulder-hand syndrome. According to their view, the great advantages of sympathetic block are the rarity of contraindications, the usually shorter period of treatment without further maintenance therapy, and the reduced likelihood of complications. The preference of these authors for stellate ganglion block appears to stem primarily from their belief that cortisone or corticotropin may foster thromboembolic phenomena in some patients, especially those with vascular disease. Steinbrocker and associates cited two possible instances of thrombotic complications caused by hormone therapy in their series but frankly admit the possibility of chance occurrence. Since the duration of treatment with these hormones varied from two to six months, a significant incidence of thromboembolism is to be expected in any group of patients with abnormalities of the vascular system who are kept under observation for this period of time. In 17 patients with shoulder-hand syndrome following acute myocardial infarction (*A.M.A. Arch. Int. Med.* **97**:487 [April] 1953), we have found the employment of cortisone to be not only highly effective but also unattended by thromboembolic complications. In 13 of these patients, cortisone was not required after a period of three weeks. This optimistic experience could also be regarded as fortuitous had it not been confirmed by further observation in an extended series. To date, my associates and I have treated 86 patients with advanced cardiovascular and/or cerebrovascular disease with cortisone and have not encountered a single instance of a thrombotic or thromboembolic incident during or after the administration of this drug. In the total group, there were 8 additional patients with shoulder-hand syndrome after acute myocardial infarction, 34 with cerebrovascular occlusion with painful disabilities complicating hemiplegia, 12 with apoplectic stroke in the acute phase of the attack, 11 with angina pectoris, 2 with acute myocardial infarction and atypical pneumonia, and 2 with congestive heart failure.

The inescapable conclusion from this experience is that the risk of thrombotic complications from the use of cortisone, even in large dosage, must indeed be small or insignificant. Moreover, there appears to be no basis for the suggestion that anticoagulants might be administered prophylactically with benefit in patients with vascular disease requiring cortisone therapy. Such preventive treatment would undoubtedly introduce a greater morbidity and mortality than that which its administration can conceivably ward off. In shoulder-hand syndrome, the excellent response to cortisone (particularly in the relief or suppression of pain), the ease of its administration, and the relative safety when simple precautions are taken lead us to believe that it should be the treatment of choice when nonspecific conservative measures fail to bring relief. The employment of stellate ganglion block, on the other hand, offers an additional approach that may prove most helpful when cortisone is ineffective or when absolute contraindications to steroid therapy exist.

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FILTERING BLOOD BEFORE TRANSFUSION

To the Editor:—There is a difference of opinion over the merits of filtering blood immediately before transfusion or administering blood to the patient through an intravenous set with a filter "in the line." In the prefiltering method, the blood is filtered by means of a closed system through a regulation filter and short length of tubing. The tubing leads into an inverted vacuum bottle. The bottle is inverted to prevent any marked agitation. The last few drops of blood from the filter are used for "rapid cell typing." The blood can then be administered through the usual intravenous set without additional filtering at the bedside. The alternate method requires that the blood be administered to the recipient with a special intravenous set having a filter in the line.

The advantages of prefiltering the blood are: 1. "Filter trouble," occasioned by clots or fibrin blocking the filter and preventing the administration of blood, is avoided. This is particularly vital in the operating room where delays can be disastrous; at the bedside it can be the cause of much exasperation and difficulty. This preliminary filtration is done in several hospitals on the request of the surgeon. These requests usually are made by surgeons who have had unfortunate experiences with "blocked" transfusions in the past. 2. It is not necessary to change the intravenous set or tubing, as the same set is used for administration of blood, sodium chloride solution, and other fluids. In patients maintained for days by intravenous therapy, frequent manipulation of the intravenous set can damage the veins and cause subsequent thrombosis. Repeated venipunctures may be difficult. Breaks in sterility are caused by these maneuvers. It is necessary to flush the tubing through with plain isotonic sodium chloride solution before and after transfusion as a precaution. Flexibility in administration of the various fluids is thus maintained. 3. The most important factor is that this technique provides an opportunity to check the type of the blood actually being administered to the recipient, right from the original container. This avoids one of the weak links in the check in operation of a transfusion service—the inability to compare the pilot tube type to the blood in the bottle. There have been no hemolytic reactions due to this sort of "confusion" since this system has been in operation.

The disadvantages of prefiltering are: 1. There is increased cost due to use of an additional vacuum bottle. 2. There is a possibility of trauma to the cells occasioned by their transfer by vacuum to the empty container. Hemolysis is avoided by inverting the receiving bottle to prevent any marked agitation of the filtered blood. It would seem that these disadvantages are minor compared to the advantage of smoother transfusions, greater flexibility in manipulation of the set, and greater safety resulting from the opportunity to type the blood actually being administered. For these reasons we prefer the technique of prefiltering blood in the blood bank immediately prior to transfusion.

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COUNCIL ON MEDICAL SERVICE

This is the 11th in a series of studies made by the Committee on Indigent Care of the Council on Medical Service concerning local plans for medical care of the indigent. A general introduction to the series and the first of the Committee's studies (Erie County, New York) appeared in the May 10, 1952, issue of THE JOURNAL, *pages 188-191. The 10th study (Richmond, Va.) appeared in the May 16, 1953, issue of* THE JOURNAL, *pages 268-270.*

Medical Care for the Indigent in Vanderburgh County (Evansville), Ind.

This is a study of medical services available to the indigent and medically indigent population of Vanderburgh County, Indiana. Of the county's 160,000 residents, 130,000 live in Evansville, an industrial center with manufacturing plants producing automobiles, refrigerators, construction machinery, and various steel, plastic, and tobacco products.

ELIGIBLE POPULATION

Table 1 shows the number of clients eligible and those actually receiving medical care during an average month under the general and public assistance programs. All those eligible for assistance under these programs are automatically eligible for medical care at public expense.

ADMINISTRATION

For years the medical care of the indigent and medically indigent of Vanderburgh County was provided on a charity basis by individual physicians. In 1947, a survey of public opinion indicated that (1) the people of the county did not know that physicians received no pay for these services and that (2) the public favored a program whereby a token payment would be made for these services. A program was subsequently devised based on a contract between the county medical society and the Department of Public Welfare and the township trustees. The society members agreed to provide medical care for all properly certified indigent and medically indigent patients in the three local hospitals in return for a monthly token payment to the society. Individual physicians may also treat public assistance clients outside the hospital, and such care, to properly certified patients, is reimbursed by the Department of Public Welfare.

The attending physician determines what medical care will be provided to public assistance patients. The committee on indigent care of the medical society supervises the medical aspects of the program. This committee establishes fee schedules and drug lists; it meets with the Department of Public Welfare monthly to review unusual or expensive cases and the methods of therapy used in such cases. Subcommittees of this group at each of the three hospitals attempt to keep hospital costs down and supervise care of the indigent in the hospital. The case workers of the welfare department certify those clients eligible under Indiana law to receive grants for old age assistance, blind assistance, and aid to dependent children. This department also administers the assistance grants for the Indiana child welfare and crippled children programs.

The general assistance programs are administered at the township level by the township trustees, elected officials who are, according to Indiana law, "the overseers of the poor." The investigators of the trustees' offices certify eligibility of the clients. There are eight townships in the county; however, since Pigeon Township includes most of Evansville and provides almost all the township assistance in the county, it is the only one whose medical program will be discussed. The Pigeon Township trustee engages one white and two Negro physicians to take care of home and office calls of general assistance clients; no payments are made to private physicians for general assistance cases treated outside the hospital. For hospital care, the township trustees have the same arrangement with the medical society as has the welfare department.

SERVICES AVAILABLE

In general, all clients of the welfare department are eligible for the same medical services. Freedom of choice of physician is provided for home and office care; hospitalized cases are under the care of the staff physicians at the hospital selected by the patient. Frequently the Department of Public Welfare learns the names of physicians on staff service at the selected hospital and sends the patient to one of these physicians for a "work-up" before hospital admittance. The attending physician may prescribe such drugs and special appliances as he feels are necessary; however, physicians are urged to use drugs on the approved list. If a drug not on this list is prescribed and exceeds by 10% or more the cost of the comparable drug on the list or is not comparable with any drug on the list, the prescription must be signed by two physicians. Prescriptions for cortisone and other expensive drugs must have the signatures of two physicians and must also be approved by the society's indigent medical care committee.

Complete dental care is available for all public assistance clients, except that old age assistance clients are not provided with dentures. Eye treatment is provided for all welfare department clients. The aid to the blind program includes remedial measures; old age assistance clients may also receive eye treatment when medically necessary. Nursing services in the patient's home are provided by the Public Health Nurses Association. Nurses are paid according to a fee schedule for such services to old age assistance and aid to the blind patients; no charge is made for aid to dependent children patients. In emergencies, the Physicians and Nurses Exchange can approve medical care for public assistance clients, since the welfare department provides this organization with up-to-date lists of all welfare recipients.

TABLE 1.—*Average Number Eligible and Receiving Medical Assistance, March, 1952 (Estimated)*

	Eligible	Recipients
General Assistance	1,847	612
Public Assistance	1,865	799
Old Age Assistance	1,465	638
Aid to Dependent Children	328	134
Aid to the Blind	72	27

The public assistance patient has freedom of choice of pharmacies, but the pharmacy must be certain of authorization before it fills a prescription. In the hospitals, no distinction is made between assistance patients and other patients; however, assistance clients are hospitalized in the least expensive rooms that medical conditions permit. All hospital facilities may be utilized for the assistance patient, including x-ray, laboratory, physiotherapy, and, at Protestant Deaconess Hospital, radioisotopic services. No restrictions are placed on the use of these services; the attending physician is the judge of the program of therapy. St. Mary's Hospital maintains a prenatal clinic that serves the indigent and also provides some postnatal services. During 1952, the clinic gave care to 58 patients on 360 visits. Protestant Deaconess Hospital maintains a crippled children's clinic for the indigent, employing the services of an orthopedist, a pediatrician, and a nurse. In addition to the officially provided services, the hospitals also care for many patients who do not qualify under one of the assistance programs but who are unable to pay for all their medical care. Patients under general and public assistance programs are cared for in nursing homes, rather than hospitals, whenever possible. Both physicians and hospitals cooperate in transferring patients to these homes as soon as medically appropriate, in order to decrease the cost of the programs. General assistance clients receive approximately the same services as public assistance clients, except for physicians' home and office calls, which are provided by the three township physicians, without freedom of choice.

PROVIDERS OF SERVICES

There are 174 physicians active in the county medical society, all of whom may provide home and office care to welfare department clients. Ninety per cent of the physicians participate in the program to some extent, although much of the work for the indigent is done by a few men. Most of the

doctors in the medical society are on the staff of at least one of the three hospitals in the county, and these staff physicians provide all in-hospital care for the indigent. Township assistance clients receive home and office care from the three contract doctors of the township. All three hospitals participate in the program. Welborn Memorial Baptist Hospital has 116 beds; St. Mary's, 178 beds; Protestant Deaconess, 245 beds. St. Mary's and Protestant Deaconess provide some specialized clinic services, but none of the hospitals maintains an outpatient department. Convalescent care is provided through 17 state-approved nursing homes in the area. The Public Health Nursing Association provides home nursing to old age assistance and aid to the blind patients at a reduced rate. All pharmacies in the area are eligible to fill assistance prescriptions.

TABLE 2.—*Monthly Payments to Medical Society*

Department of Public Welfare	$300.00
Pigeon Township	750.00
Knight Township	150.00
Perry Township	120.00
Center Township	70.00
Two townships	7.50 each
Two townships	No payment
Total	$1,405.00 monthly
	$16,860.00 annually

PAYMENT FOR SERVICES

For the in-hospital care rendered by physicians, the Department of Public Welfare and six of the eight township trustees make monthly token payments to the Vanderburgh County Medical Society; the two townships that make no payment are too small and too poor to afford such payment. Table 2 shows the various monthly contributions; since Pigeon Township is the county's largest and contains most of the county indigent, it contributes more to the society than all the other townships together.

Private physicians who provide medical care to certified public assistance patients on home or office calls are paid by the welfare department according to a fee schedule agreed upon by the society's committee on indigent medical care and the welfare department. In January, 1954, the welfare department will begin limiting calls, whether home or office, to three per month unless prior authorization is obtained. The township trustee engages the services of one white and two Negro physicians to provide home and office care for general assistance clients. The white physician receives a salary of $225 per month, while the Negro physicians are paid $3.00 for each office call and $4.00 for a home call. Hospitals give no discounts for assistance patients but charge the Department of Public Welfare and the township trustees the full hospital rates for care rendered to indigent patients. Pharmacies also receive the full retail price for prescriptions; bills are presented monthly.

TABLE 3.—*Average Cost of Public Assistance Medical Care Per Month*

Program	Cost per Mo.	Per Eligible Client	Per Recipient
Old Age Assistance	$19,377.98	$13.23	$30.37
Aid to Dependent Children	2,571.42	7.84	19.19
Aid to the Blind	413.86	5.75	15.33
	$22,363.26	$11.99	$27.99

COSTS AND FINANCIAL SUPPORT

The expenditures of the Department of Public Welfare for the public assistance medical programs are given in table 3.

In addition to these expenditures, the department also supervises 72 children in foster homes; medical care for these children totaled $593.51 during the month of March, 1952. Pigeon Township provides approximately 80% of the general assistance care of the county; during 1952, 126 major operations and 38 minor ones were performed for indigent residents of the township under this program. The estimated value of medical services given by physicians to the indigent of all townships in the county during 1952 amounted to $45,000. The annual cost for medical care for assistance patients is shown in table 4.

The costs of the public assistance program are met by the state, with matching federal grants up to a monthly maximum of $55.00; the Department of Public Welfare's average assistance grant is less than this maximum. All funds necessary for medical care, in addition to those contributed by the state and federal governments, are provided by the state and county on a 60:40 ratio. Township funds to meet general assistance costs are raised by means of general property taxes.

SUMMARY

Vanderburgh County provides medical care for its indigent and medically indigent through a program based in part on contracts with the county medical society. Public and general assistance clients receive in-hospital care from staff physicians in return for a token monthly payment to the society; the payment is used to carry on society activities. All three of the county's hospitals are utilized in the two programs, and hospitals are paid full rates for their services. Both programs also use the county's 17 nursing homes and pay full retail prices for prescriptions, which may be filled at any pharmacy. The programs differ in nonhospital care: the welfare department's clients may receive home and office care from any physician and the physician will be reimbursed according to a fee schedule prepared by the society and the welfare department. The township trustees, who administer the general assistance program, provide home and office care through contract physicians.

TABLE 4.—*General Assistance Medical Costs Including Hospital Care, Pigeon Township, 1952*

Hospitalization		$71,342.58	
Out-patient care		667.35	
Payment to medical society		9,000.00	
Estimated value, hospital staff care			$35,000.00
		$81,009.93	
Total admissions	303		
Patient days	3,871		
Average stay	12.78 days		
Average cost per patient day		$20.93	

Public assistance clients must be certified as eligible by the welfare department before they can receive care. However, in emergencies when the department is not open, the Physicians and Nurses Exchange maintains an up-to-date list of welfare clients, so that physicians and hospitals can determine whether care is authorized at any time of day or night. General assistance clients must depend for emergency care on the township physicians and the hospital emergency rooms. Medical aspects of the program are supervised by the county medical society's indigent care committee, which helps work out fee schedules and approved drug lists, reviews and authorizes expensive procedures, and, through three subcommittees, helps keep down costs at the three hospitals.

The program seems to be operating to the satisfaction of the county medical society and the welfare department; 90% of the society members are participating to some extent. However, the township trustee is dissatisfied with the high cost of the program though not with the quality of care provided. The division of the county into eight townships, with each township responsible for its own indigent, causes some administrative shortcomings, such as the duplication of administrative functions and the variance in the amount of funds available for care in contiguous townships. As the township trustee is an elected official, and the responsibility for general assistance medical care is not spelled out in detail in the laws, a change in officials can give rise to some fluctuation in policy and services provided. An additional shortcoming in the township program is the lack of freedom of choice of physicians. Much of the success of the program is due to the physicians' interest in it. The society's indigent care committee has met with cooperation and success in the devising of and use of fee schedules and approved drug lists, and all agencies involved cooperate in keeping costs of the programs to a minimum.

BUSINESS PRACTICE

The following material is based on a public relations manual issued by the Public Relations Department of the American Medical Association.—ED.

RENDERING OF BILLS

In the past years doctors' bills were sent out bearing this familiar phrase, "For Professional Services," the sum owed, and nothing more. Often bills were mailed irregularly, if at all. Today patients expect to receive statements of their obligations. Most families plan their budgets around bills received on or about the first of the month. The physician is responsible

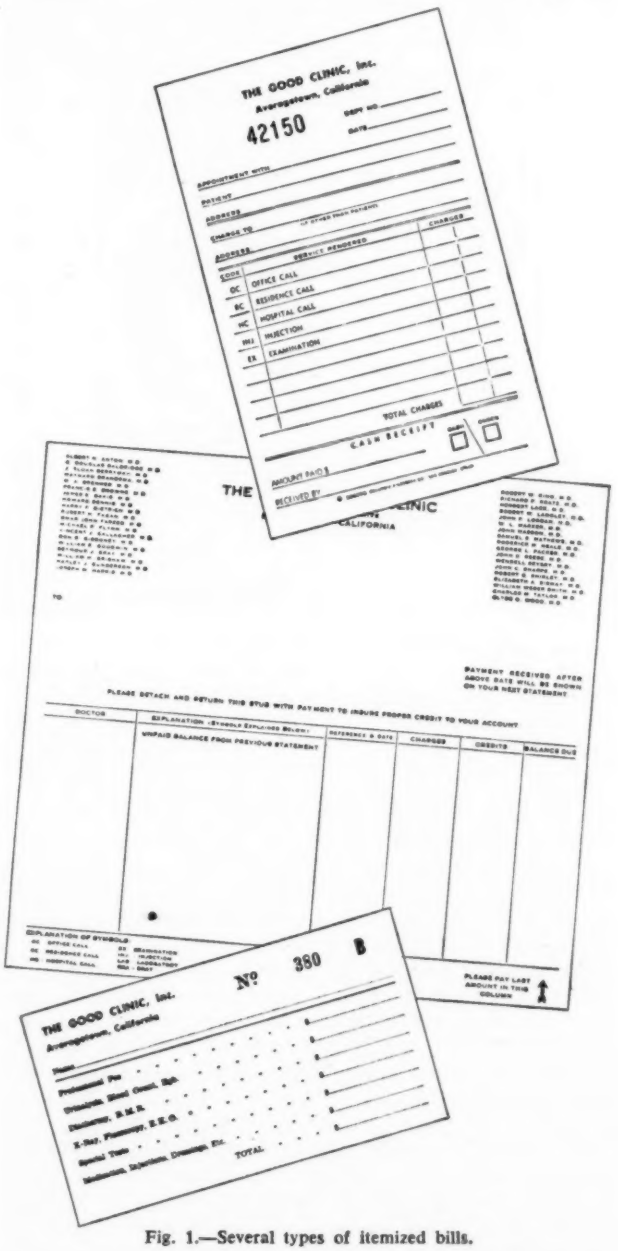
THE GOOD CLINIC, Inc.
Averagetown, California
42150
CASH RECEIPT
TOTAL CHARGES
PLEASE DETACH AND RETURN THIS STUB WITH PAYMENT TO INSURE PROPER CREDIT TO YOUR ACCOUNT
PAYMENT RECEIVED AFTER ABOVE DATE WILL BE SHOWN ON YOUR NEXT STATEMENT
THE GOOD CLINIC, Inc.
Averagetown, California
No 380 B
TOTAL

Fig. 1.—Several types of itemized bills.

for explaining in advance fees, including additional bills from other members of the medical team such as assistant surgeons and anesthetists, and for sending bills at regular intervals with charges itemized. The best way to explain medical charges is by itemizing medical bills. Patients are entitled to know what charges are for. As time elapses after treatment, the patient may forget that he was treated four times instead of three times. On the surface of an unitemized bill, it may appear to the patient that he has been overcharged. The simplest way to itemize bills is to allow space on the original statement below the "For Professional Services" line on which the secretary can list the separate charges for office, house, or hospital calls or for tests and treatment (fig. 1).

A regular system of rendering statements should be used. Statements should be sent at least once each month. Some physicians send bills after treatment has been given; others bill at the first of each month. Others find it more satisfactory to mail statements on the first and the 15th of each month or to use the cyclical billing system used by department stores. Under this plan, statements are sent out to patients whose last names begin with certain letters of the alphabet on certain dates of each month, i. e., patients with names beginning with A through G receive statements on the first, patients with names beginning with H through N receive statements on the fifth, and so forth. Punctuality in billing encourages prompt payment. The use of self-addressed business

Fig. 2.—Itemized "charge slips" that may be given to the patient before he leaves the doctor's office or may be mailed in a combination statement-reply envelope.

reply envelopes (fig. 2) also encourages punctuality. If the physician is negligent and does not send a bill for several months after treatment, the patient may justifiably deduce that the doctor does not attach much importance to the bill and postpone payment, sometimes indefinitely. Patients also are entitled to know the date on which payment of their medical bills is due.

When payments are sent in by check, it is not absolutely necessary for the doctor's secretary to mail a receipt, because the patient retains his check stub as evidence of payment. On the other hand, a thank-you note sent on receipt of payment goes a long way in promoting a better doctor-patient relationship. Cash payments received by mail should always be acknowledged promptly. Regular billing and itemizing of statements not only is a service to patients but is valuable to the physician, since prompt payments are usually forthcoming if these practices are followed.

THE LEISURE CORNER

TOOLS AND RULES FOR AMATEUR DESIGNERS

Many physicians gravitate to hobbies that require manual dexterity by virtue of their temperament, inclination, or aptitude. Cultivation of an interest in the handicrafts, they have found, depends on the attainment of aesthetic enjoyment as well as on actual manual accomplishment. This article, the first of a series to be devoted to various handicrafts, will attempt to familiarize the reader with basic concepts of decoration and ornament, with which to give both distinction and character to any structural form. What follows will be an elementary discussion of the tools and rules that will enable the prospective hobbyist to create decorative designs appropriate for use in any one of a number of handicraft fields. For purposes of clarification, distinction should be made between structural and decorative design. Structural design represents the form, proportion, and utility of an object. Generally speaking, one can accept structural design as being the contour line or the outline of the object. Decorative design, on the other hand, is that something that is added to or on the surface of a structural design without altering the shape, contour, or outline of the object. It represents that added beauty that a product might not otherwise possess, and it is that something extra that distinguishes articles of similar structure. Actually, a good decoration is no more than a pleasing arrangement of line, mass, and color. The lines that form the masses and the principles that make them pleasing when used in composition represent the tools and rules that are suitable for use by the amateur designer.

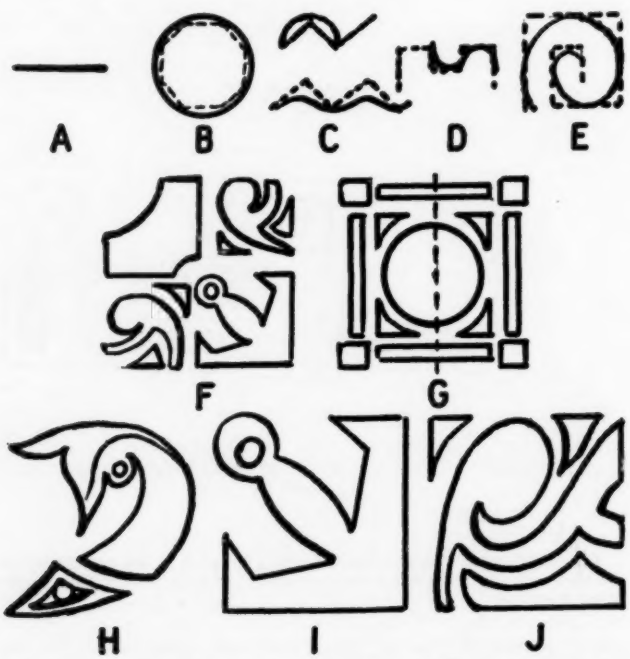

Fig. 1.—A—E, basic lines or tools. *C* shows zigzag, half circle, and wave. F—J, rules or principles demonstrated. See also fig. 2.

A logical place to begin the discussion of tools is with the straight line (fig. 1, *A*). It is very easy to visualize straight lines in combination, joining at angles of varying degrees so as to produce a triangle, square, hexagon, or octagon (*B*). If preferred, straight lines can be combined in chain-like fashion to produce a zigzag line (*C*) or embattled (*D*), appropriate for a border pattern. Still another variation is to start a straight line as if to outline a large square. After completing three sides, the fourth side is shortened and subsequent lines designed to form smaller squares within the original so as to produce the fret pattern (*E*). The octagon, zigzag, embattled, and fret provide the designer with the geometric basis by which necessary curved forms are developed to break the monotony of straight lines in a composition. In rounding off the corners of these figures, a curved series is developed. The octagon becomes a circle (*B*), the zigzag develops into a half circle or wave (*C*), the embattled produces the reverse curve (*D*), and the fret generates the spiral (*E*).

The rules for the amateur designer are those that govern natural and abstract composition alike. Good ornament can be achieved only by their use.

Proportion.—A pleasing proportion is achieved through the use of certain ratios between the various dimensions of masses, regulated distances between lines, and alternations between ornament and plain or background surface. Proportion, then, is harmony between parts of the ornament as well as between ornament and background (fig. 1, *F*).

Fig. 2.—An ornament in which basic lines and principles are used.

Balance.—Pleasing balance is achieved in one of two ways. It can be symmetrical (fig. 1, *G*), derived "likesidedness" from doubling of any form on its axis, by absolute similarity on both sides of a piece of ornament. It can also be unsymmetrical (fig. 2), wherein similarity does not exist on each side of the ornament, but where different masses nevertheless appear to be of equal weight.

Emphasis.—A pleasing design must have a motif, an idea that dominates the composition and can be identified without appearing to stand alone. It is restful as opposed to harsh or strong contrast between motif and supporting masses (fig. 1, *H*).

Contrast.—A pleasing composition avoids monotony. It opposes a straight line with a curve and accomplishes a difference in form and arrangement without disturbing a restful feeling and an easy flow of lines and mass (fig. 1, *I*).

Unity.—A pleasing design shows perfect accord in all parts. Regardless of the variety of lines and masses employed, all elements must appear to belong to each other (fig. 1, *J*).

This discussion would not be complete unless tools and rules were utilized to produce an ornament. For example, a structural form is presented that might very well represent the side of a leather handbag (fig. 2). Here is demonstrated an occasion where it is desirable to divide the over-all space into smaller areas. Interest in corner and border arrangement is achieved by the breaking up of the main area. It will be observed that these smaller areas are, nonetheless, pleasing and bear a relationship to each other and to the contour of the structural mass. In contrast to the left half of this design, which demonstrates only division of space, the right half continues to develop the ornament to completion.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A Arch. Neurology and Psychiatry, Chicago

70:413-550 (Oct.) 1953

*Quantitative Test of Theory and Diagnostic Indicators of Childhood Schizophrenia. L. Bender and W. H. Helme.—p. 413.
Neuropsychiatric Aspects of Infantile Eczema: Special Reference to Role of Cutaneous Pain Receptors. M. J. Rosenthal.—p. 428.
*Use of Electric-Convulsive Therapy in Morphine, Meperidine, and Related Alkaloid Addictions. F. B. Thigpen, C. H. Thigpen and H. M. Cleckley. —p. 452.
Prognosis in Psychiatry: Results of Psychiatric Treatment. K. E. Appel, J. M. Myers and A. E. Scheflen.—p. 459.
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Bulbar Reticular Formation and Tremor. F. L. Jenkner and A. Ward Jr. —p. 489.
Role of "Body Image Concept" in Pattern of Ipsilateral Clinical Extinction. R. Cohn.—p. 503.
Use of Phenacemide (Phenurone) in Treatment of Narcolepsy and Cataplexy: Preliminary Report. R. B. Aird, N. S. Gordon and H. C. Gregg.—p. 510.
Electroshock and Rat Adrenal Cortex. J. R. Royce and H. E. Rosvold. —p. 516.

Indicators of Childhood Schizophrenia.—Over two decades (1934-1952) about 7,000 children referred to the psychiatric division of Bellevue Hospital were examined, tested, observed, and referred to homes and institutions for more permanent care. Those who worked with these children had a variety of backgrounds, psychoanalytic, neuropsychiatric, behaviorist, Gestalt. Their concern for the care of the child in the immediate situation was perhaps the one factor they held in common. Out of this diversity of views, a theory has become more integrated, and, with the improvement of diagnostic measures and observation techniques, it appeared feasible to formulate the theory in such a way as to permit objective tests of its working hypotheses. This report describes the results obtained in the first step toward verification. As a check on specific hypotheses arising from the theory, the case records of 30 schizophrenic and 30 nonpsychotic disturbed children were analyzed. One hundred thirty-eight items were rated and recorded by a team of two psychiatrists, a social worker, and a psychologist. Sources of information were psychiatric interviews, notes of nurses and ward personnel, physical and psychological examinations, and interviews with parents. Items were classified in the areas of vasovegetative and motor functioning, body image and self-world perceptions and reality testing, anxiety and neurotic symptoms, social responses, responses to authority, sex expression, and intellectual functioning. Specific predictions on the items were made in advance. Statistical confirmation of these was high, full confirmation ranging from 60 to 79% and full or partial confirmation in some areas from 77% to 88%. The confirmation figures yield possibly a minimal estimate of validity of the hypotheses, since categories were necessarily coarse. The next major steps contemplated are: (1) refining and retesting the recordings on a larger population of more recent date in which the original diagnoses have been confirmed by follow-up study and (2) setting up a standard recording system for current cases for a more systematic checking of major propositions in the theory. The following characteristics of childhood schizophrenia were supported by this study: 1. Childhood schizophrenia is characterized by a disturbance in the regulation of maturation processes at both biological and psychological levels. 2. The dominance of tonic-neck-reflex motility is a particularly striking example of the maturational lag and unevenness of development. 3. The schizophrenic child has basic difficulties in boundaries and segregation of physiological and psychological subsystems. 4. The disorder pervades to some extent virtually all major areas of functioning, in contrast to the concentration of symptoms in single areas among neurotic children and those with primary behavior problems. 5. The concept of plasticity characterizes the behavior and organization of the schizophrenic child in virtually all these areas.

Electroshock Therapy in Drug Addiction.—Attempts have been made to alleviate the manifestations of drug withdrawal by administration of corticotropin or cortisone. Recent reports indicate that little or no relief is afforded by these hormones. The Thigpens and Cleckley began to use electric convulsive treatment in 1948, and the method proved highly successful in controlling the emotional and physiological disturbances during withdrawal. Kalinowski and Hoch reported similarly gratifying results and pointed out that years earlier pentylenetetrazol (Metrazol) shock had been found useful. The authors list 35 drug addicts representative of a larger group treated with electric convulsive therapy. The majority of the patients were addicted to morphine, meperidine, and codeine, singly or in combination, and the duration of addiction ranged from a few months to 20 years. The number of electric convulsive treatments varied. In cases of severe addiction, the authors often give three or four treatments during the first 24 hours. On the second day, two or three may be necessary. After this, one treatment daily is likely to suffice over a period of several days. Then a single electroshock treatment on alternate days usually keeps the patient free of distress. Rarely is it necessary to continue therapy beyond the second week of hospitalization. Confusion from the treatment, particularly during the early days, seems to be desirable, since this plays a part in combating the psychic or emotional component of the withdrawal reaction. The authors reject as unfounded the charge made by some that electroshock therapy is destructive and brutal and point out that the physiological stresses of withdrawal are far more likely than electric convulsive therapy to precipitate coronary thrombosis or to diminish resistance to infection. The possibility of suicide during the despair and misery of withdrawal constitutes a more serious risk to life than the electroconvulsive therapy. Skeletal injury from electric convulsive therapy can be avoided by the use of succinylcholine, which has proved to be a safe, reliable, and effective agent for producing muscular relaxation.

A.M.A Arch. Pathology, Chicago

56:231-332 (Sept.) 1953

Protective Influence of Pregnancy on Experimental Collagen Disease Lesions. R. L. Holman and C. K. Jones.—p. 231.
Aging Processes of Aorta and Pulmonary Artery in Negro and White Races: Comparative Study of Various Segments. S. H. Gray, F. P. Handler, J. O. Blache and others.—p. 238.
Subacute Cerebral Fat Embolism Complicated by Juxtaembolic Thrombosis of Fibrin. J. Cammermeyer.—p. 254.
Effect of Aureomycin on Experimental Arteriosclerosis and Serum Cholesterol Levels. D. Nelson, A. C. Ivy, R. Altschul and R. Wilheim.—p. 262.
Experimental Endocarditis in Normal Animals and in Animals Treated with Cortisone. B. J. Clawson.—p. 268.
Observations on Thyroid Colloid. R. R. Fisher.—p. 275.
Hypertension in Bilaterally Nephrectomized Dogs in Absence of Exogenous Sodium Excess: Maintenance of Fluid Balance During Peritoneal Irrigation. E. E. Muirhead, F. Jones and P. Graham.—p. 286.
Hematoxylin Bodies Associated with Allergic Angiitis in Absence of Lupus Erythematosus. B. Worken and R. D. Pearson.—p. 293.
Sarcoma of Endometrial Stroma. W. B. Ober and R. S. Jason.—p. 301.

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Titles marked with an asterisk (*) are abstracted.

American J. Digestive Diseases, Fort Wayne, Ind.

20:251-292 (Sept.) 1953

Constancy of Acid Values in Series of 227 Peptic Ulcer Cases Studied by Repeated Gastric Analyses. S. Morrison and M. Feldman.—p. 251.
Gastric Ulcer: Its Diagnosis and Differentiation by Gastroscopic and Roentgenologic Examination. L. L. Hardt, F. Steigmann and A. Weiss. —p. 253.
Concept of Periodicity in Natural History of Peptic Ulcer and Its Consequences. R. Jahiel.—p. 257.
Obesity: Overnutrition or Disease of Metabolism. A. W. Pennington. —p. 268.
Alpha Cells of Pancreatic Islets and Pathogenesis of Diabetes Mellitus. M. Fabrykant.—p. 275.
Effect of Gastric Secretory Depressants (Banthine, Bellafoline and Amidopyrine) on Innervated Gastric Pouch in Dogs. L. J. Notkin, R. A. Forse and D. R. Webster.—p. 277.
Primary Adenocarcinoma of Appendix. H. J. Epstein, T. H. Mendell and A. S. Conston.—p. 284.

American Journal of Medical Sciences, Philadelphia

226:357-476 (Oct.) 1953

Penicillin Reactions: Their Nature, Growing Importance, Recognition, Management and Prevention. R. A. Kern and N. A. Wimberley Jr. —p. 357.
Correlations in Clinical and Epidemiological Investigation. T. Francis Jr. —p. 376.
Observations on Natural History of Gastric Cancer. L. E. Meiselas. —p. 383.
*Pulmonary Manifestations of Disseminated Lupus Erythematosus. H. L. Israel.—p. 387.
Interstitial Pneumonia and Focal Myocarditis in Poliomyelitis. S. S. Jurow and V. B. Dolgopol.—p. 393.
Management of Shock in Myocardial Infarction with l-Norepinephrine. D. G. Calenda, J. F. Uricchio and L. M. Friedman.—p. 399.
*l-Triiodothyronine Versus l-Thyroxine: Comparison of Their Metabolic Effects in Human Myxedema. R. W. Rawson, J. E. Rall, O. H. Pearson and others.—p. 405.
Incidence and Significance of Sickle Cell Disease in Deaths Subject to Medicolegal Investigation. G. W. Thoma.—p. 412.
Comparison of Effects of Terramycin Hydrochloride and Amphoteric Terramycin on Fecal Flora of Humans. S. A. Broitman, J. R. Cohen and W. Litsky.—p. 419.
Treponemal Immobilization Test. H. Beerman.—p. 425.
Present Status of Surgical Treatment of Ménière's Disease. A. H. Neffson. —p. 442.

Pulmonary Manifestations of Disseminated Lupus Erythematosus.—Roentgenologic or pathological evidence of pulmonary or pleural disease was noted in 20 of 22 patients with disseminated lupus erythematosus. Nine patients died and necropsies were performed. Fifteen patients exhibited on one or more admissions clinical and roentgenologic evidence of pneumonia; in two other patients, previously unsuspected pneumonia was observed on necropsy. Roentgen studies disclosed diffuse perivascular or vascular changes considered characteristic of the collagen disease in only one patient. Two patients had pleurisy with large effusion. Roentgenologic examination disclosed lobar consolidation in some patients with frank symptoms and signs of pneumonia. More often, the respiratory symptoms were overshadowed by the systemic toxemia. Physical signs were minor; in such cases the roentgenologic appearance was usually that of patchy pneumonia. Sputum cultures yielded mixed growths of the common respiratory tract organisms, including pneumococci and streptococci. It appears that pulmonary involvement is extraordinarily frequent in disseminated lupus erythematosus and, therefore, cannot be considered coincidental. Specific pulmonary lesions, comprising either disseminated perivascular changes or chronic interstitial pneumonia, and masssive pleural effusion are relatively infrequent. The commonest manifestation is a nonspecific pneumonia that occurs as a terminal event, but is also frequently a recurrent or migrating process. Disseminated lupus may occasionally be present with predominantly respiratory manifestations. A search for the lupus erythematosus phenomenon should be made in patients with recurrent pneumonia, infiltration, or pleurisy of uncertain cause.

Metabolic Effects of *l*-Triiodothyronine and *l*-Thyroxin in Myxedema.—The total metabolic effects of *l*-triiodothyronine and of *l*-thyroxin were compared with those of *l*-diiodothyronine in a 41-year-old woman with classic myxedema. All urines and stools of the patient were saved for analysis of sodium, potassium, calcium, phosphorus, and nitrogen. The urine was assayed daily for creatine and creatinine. The basal metabolic rate of the patient was determined daily. *l*-Diiodothyronine in the dose of 1 mg. had no significant effect on the basal metabolic rate or on the excretion of nitrogen, phosphorus, and creatine. *l*-Triiodothyronine exerted a prompt but short-lived increase in the basal metabolic rate and in the excretion of nitrogen, phosphorus, and creatine. *l*-Thyroxin exerted a slow and prolonged effect on the same indices. If one disregards time of action, there were no qualitative differences between these two agents. Quantitatively, on an equimolar basis, the only difference is in the speed of action. The difference in the speed of action of *l*-triiodothyronine and *l*-thyroxin can be correlated with the rate of disappearance of each of these hormonal preparations from the circulation.

American Journal of Obstetrics & Gynecology, St. Louis

66:697-928 (Oct.) 1953. **Partial Index**

*Cortisone in Treatment of Hirsute Woman. R. B. Greenblatt.—p. 700.
Experience of Savannah Tumor Clinic in Carcinoma of Stump of Cervix. A. J. Kelley and D. L. Brawner.—p. 711.
Mixed Mesodermal Tumors of Uterus. L. A. Wilson Jr., L. Graham Jr., W. N. Thornton Jr. and J. M. Nokes.—p. 718.
Problem of Uterine Fibroid. N. F. Miller, P. P. Ludovici and E. Dontas. —p. 734.
Trend in Cesarean Section in Recent Years. O. H. Jones.—p. 747.
Puerperal Inversion of Uterus. J. E. Bell Jr., G. F. Wilson and L. A. Wilson.—p. 767.
Symphysiotomy Versus Difficult Forceps. J. Ortiz-Perez.—p. 781.
Secondary Dysmenorrhea. F. H. Falls.—p. 816.
*Treatment of Female Genital Tuberculosis with Streptomycin and *p*-Aminosalicylic Acid. H. Sered, F. H. Falls and B. P. Zummo. —p. 823.
Veratrum Treatment of Toxemia of Pregnancy: Controlled Study. F. A. Finnerty and G. J. Fuchs Jr.—p. 830.
Treatment of Stress Incontinence in Female. J. C. Ullery.—p. 853.
Pregnancy and Hodgkin's Disease: Report of Eight Cases. H. L. Riva, P. S. Andreson and J. W. O'Grady.—p. 866.
Cytological Detection of Uterine Cancer in Private Obstetrical and Gynecologic Practice: Based on Analysis of 104 Consecutive Positive and Suspicious Smears from 8,148 Patients. T. A. Slate, P. L. Martin and J. W. Merritt.—p. 878.
Acute Sodium Deficiency in Postpartum Pre-Eclamptic Patient: Report of Case. D. L. Hutchinson and A. A. Plentl.—p. 891.

Cortisone in Treatment of Hirsute Woman.—Twenty-seven women, 15 of whom also had amenorrhea, 6 irregular menses, 4 regular menses, and 2 previous hysterectomies, were treated with 50 mg. of cortisone given orally every day for from 2 to 18 months. In two women of the first group treatment was discontinued within one to two months because of untoward effects such as depression and melancholia. No change in menstrual function occurred in two patients of the first group, in two of the second, and in all four of the third. The number of ovulations increased in eight of the first group and in four of the second. The number of anovulatory menses increased in three of the first group. A very mild improvement in the hirsutism occurred in four of the first group, one of the second, one of the third, and both of the fourth. In comparing these cases with his previous experiences in the treatment of hirsute amenorrheic women by ovarian resection, the author finds that the patients who experienced little benefit after surgery were significantly aided by further cortisone therapy, while some of the patients who failed to respond to cortisone were benefited by ovarian resection. He postulates a threefold distribution of types of disorders: primarily ovarian, primarily adrenal, and due to an imbalance in the pituitary-adrenal-ovarian axis. The finding of hirsutism, menstrual disorders and mild to moderate elevation of urinary 17-ketosteroids may be common to most cases in these groups, but it is difficult to classify them categorically as belonging to one or another group. The author thinks that excess androgen production in these cases may come from either the excessively luteinized (hyperthecosis) ovaries or from the adrenal cortex or from both sources. If this concept is acceptable, it explains why cortisone helps one group, ovarian resection another, and combined methods a third. The physiological role of cortisone in the management of the hirsute woman may have its effect not merely on the depression of 17-ketosteroid excretion through its inhibition of corticotropin (ACTH) production, but on the balance of growth hormone and adrenal steroids so as to permit a more orderly release of pituitary gonadotropins.

Treatment of Female Genital Tuberculosis with Streptomycin and Para-Aminosalicylic Acid.—Clinical evidence indicates that dihydrostreptomycin when used with *p*-aminosalicylic acid (PAS) is superior to treatment with either of these drugs alone. Combined therapy is superior because the development of resistant bacterial strains is inhibited or significantly delayed; both drugs possess bacteriostatic and possible bacteriocidal effects, and are able to be tolerated over longer periods of time. Para-aminosalicylic acid may be used for its suppressive effects long after the tubercle bacilli have become resistant to streptomycin. It also lessens the possibilities of relapses and recurrences. The patient's own powers of recovery are increased by combined therapy, and, if surgery eventually becomes necessary, the patient is better prepared for it. In a series of 18 consecutive female patients with genital tuberculosis, combined therapy was used to determine whether or not surgery can be eliminated in the treatment of this disease. The average dose of streptomycin was 1 gm. daily given in a single intramuscular injection. The dosage of *p*-aminosalicylic acid was 10 gm. daily. The duration of combined drug therapy was as a rule three and a half to four months. It was found that the need for surgery is sometimes eliminated in some forms of the fibroplastic types of genital tuberculosis with or without ascites, but that the advanced forms of hyperplastic genital tuberculosis and/or caseous lesions usually necessitate extirpational procedures. The clinicopathological peculiarities of tuberculosis are such that the diagnosis may easily be missed; 5 of these 18 patients were subjected to initial surgery with a diagnosis other than genital tuberculosis. In the other 13, diagnoses were correct, and they were managed accordingly. Abdominal distention with or without ascites, appearing within a few months after abortion or delivery, should strongly suggest the possibility of the disease. The recent introduction of the isonicotinic acid hydrazides does not minimize the value of combined *p*-aminosalicylic acid and streptomycin therapy, since there is evidence that the tubercle bacilli often show increasing resistance to the hydrazides.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

70:543-704 (Oct.) 1953

*Significance of Solitary Mass in Lung. C. A. Good, R. T. Hood and J. R. McDonald.—p. 543.
Insulo-Opercular Arteries of Brain, with Special Reference to Angiography of Striothalamic Tumors. B. Schlesinger.—p. 555.
Roentgen Demonstration of Semicircular Canals in Paget's Disease. K. Kettunen.—p. 564.
Roentgenologic Aspects of Lethal Granulomatous Ulceration of Midline Facial Tissues. R. M. Geist, Jr. and W. H. Mullen, Jr.—p. 566.
Post-Traumatic Diaphragmatic Herniation of Segment of Liver Simulating Anomalous Lobe of Liver. M. Shoshkes and F. J. Lovelock.—p. 572.
Traumatic Mediastinal Hematoma. Z. F. Endress.—p. 576.
Simulated Color Roentgenography. A. H. Dowdy and L. J. Bonann.—p. 581.
Preliminary Evaluation of New Cholecystographic Medium, Teridax. C. R. Weinberg.—p. 585.
Cancer of Larynx Treated by 500 Kilovolt Roentgen Rays. J. S. Binkley.—p. 591.
Physiopathologic Study of Effect of Radioactive Iodine on Ovary. F. W. Tillotson, R. G. Rose and S. Warren.—p. 599.
Multiple Scintillation Counter in Vivo Scanner. H. O. Anger.—p. 605.
Distribution and Excretion of C^{14} Methyl Labeled Glycine. G. L. Nardi.—p. 613.

Significance of Solitary Mass in Lung.—The preoperative roentgenograms of 156 patients who underwent surgical removal of a solitary circumscribed mass in the lung provided the basis for this study. Postoperative analysis of material from the lesion showed 55 to be malignant. A review of the diagnostic evidence revealed that symptoms described by the patient, laboratory tests, skin tests, cytological examination of sputum and bronchial washings, and bronchoscopy did not provide conclusive evidence of either malignant or benign character of the masses. Only the roentgenologist can discover the one positive indication of benignancy—calcification of the mass. Since this is the only definite contraindication to surgery, apart from the general condition of the patient, relative certainty that the lesion is a metastatic extension of a disease known to be present, or suspicion of a benign lesion based on the youth of the patient, the role of the roentgenologist becomes extremely important in the treatment of a solitary mass in the lung.

Am. Practitioner & Digest of Treatment, Philadelphia

4:679-744 (Oct.) 1953

Chronic Renal Failure. A. J. Merrill.—p. 679.
Roentgen Ray Treatment of Leukemia: Therapeutic Paradox. I. Sussman.—p. 686.
Diagnostic Approach to Patient with Anemia. S. O. Schwartz.—p. 690.
Physician and Alcoholism. M. A. Block.—p. 694.
Headache Clinic V: Tension Headache. L. S. Blumenthal, M. Fuchs and A. B. Bennett.—p. 701.

American Surgeon, Atlanta, Ga.

19:915-1014 (Oct.) 1953

Experimental Vascular Grafts: II. Some Undesirable Gross and Microscopic Changes Observed in Arterial Homografts After Implantation into Thoracic Aorta of Growing Pigs: Preliminary Report. E. A. Kanar, L. M. Nyhus, E. J. Schmitz and others.—p. 915.
Surgery as Palliation in Terminal Malignancy Patient. J. T. Payne.—p. 924.
Treatment of Venous Insufficiency of Lower Extremities with Note on Use of Ascending Phlebography. E. D. Grady and E. M. Colvin.—p. 936.
*Bile Peritonitis—Sequelae and Treatment. D. L. Maguire Jr.—p. 946.
Wound Complications Following Surgery. H. T. Whitaker and J. W. Lamb.—p. 953.
Surgical Treatment of Patent Ductus Arteriosus. W. K. Swann and T. L. Lomasney.—p. 964.
Pulmonary Complications Following Upper Abdominal Surgery. F. T. Kurzweg.—p. 967.
Surgical Therapy for Pulmonary Coccidioidomycosis. P. H. Guilfoil.—p. 975.
Surgical Treatment of Degenerative Arthritis of the Hip. F. C. Reynolds.—p. 981.
Emotional Aspects of Surgical Practice. C. K. Hofling.—p. 989.
Carcinoma of Cecum Associated with Acute Appendicitis: Case Report. E. K. Robinson and R. W. Ernst.—p. 1000.
Review of Diagnosis and Treatment of Toxic Goiter. L. A. Bible.—p. 1005.

Bile Peritonitis.—Maguire believes that many more cases of bile peritonitis have occurred than have been reported. The commonest causative factor is rupture of the common bile duct. Less frequently, bile peritonitis may follow leakage from accessory hepatic ducts after cholecystectomy or perforation of the gallbladder or as a result of rupture of the liver or of extra hepatic biliary system either by intra-abdominal injury, such as stab or gun shot wounds, or extra-abdominal injury from a blow or a fall. Usually, the biliary soiling of the peritoneal cavity is sudden. The patient's peritoneal surfaces are flooded with a chemical irritant within a short time. Added to this is the fact that probably in the majority of cases the bile is infected, so that the surgeon is confronted with a suddenly and desperately ill patient who is convalescing from a cholecystectomy and/or choledochostomy and who has a superimposed septic generalized peritonitis. This explains the 60% mortality rate cited on this complication. Rupture of the common bile duct with resultant bile peritonitis may occur at any time after cholecystectomy or choledochostomy. It has been reported as early as 12 days and as late as three and a half years after such operations. Since the outcome is almost certainly fatal without operation, the abdomen should be opened at the earliest moment the diagnosis appears probable. The bile is evacuated; drains are inserted, and, if feasible, the common duct is intubated. The patient is supported with the routine peritonitis regimen. It is wise not to use morphine, since this drug tends to increase sphincter spasm. The author presents a case history of bile peritonitis to illustrate some of the complications that may result. The condition should be suspected in anyone who presents signs of generalized peritoneal irritation with varying degrees of collapse following cholecystectomy and/or choledochostomy. If the patient survives the acute episode, the condition may continue into the subacute or chronic phase, characterized by localized bile collections and/or partial or complete intestinal obstruction due to adhesions. Biliary fistulas following drainage of localized pockets frequently will heal spontaneously. If not, excision of the tract, with the diseased portion of the common duct, may be necessary. Obstruction, usually seen in the duodenum or upper jejunum, may require mobilization or anastomosis around the involved segment of bowel.

Arizona Medicine, Phoenix

10:311-352 (Sept.) 1953

Development of Medical Use of Radioisotopes. P. C. Aebersold.—p. 311.
Breast Lesions as Seen in Physician's Office. H. H. Davis.—p. 316.

10:353-382 (Oct.) 1953

Indications for Irradiation of Breast Lesions. U. V. Portmann.—p. 353.
Role of the Non-Specialist in Care of Allergic Disease. S. M. Feinberg. —p. 354.
Why Report Communicable Diseases? C. G. Salsbury and J. B. Swayne. —p. 358.

Arkansas Medical Society Journal, Fort Smith

50:77-94 (Oct.) 1953

The Tuberculosis Problem in Arkansas. J. D. Riley.—p. 78.
Post-Operative Care to Prevent Recurrence of Kidney Stones. G. Carroll. —p. 80.
Recent Trends in Diagnosis of Cancer. J. H. Growdon.—p. 83.
"Fluid Balance—Everyone's Specialty." A. Kahn Jr.—p. 85.

Bulletin of Johns Hopkins Hospital, Baltimore

93:147-204 (Sept.) 1953

*Local Use of Hydrocortisone Acetate: Preliminary Report. R. C. V. Robinson.—p. 147.
Diagnosis and Surgical Removal of Intracavitary Myxoma of Right Atrium. H. T. Bahnson and E. V. Newman.—p. 150.
Comparison of Metabolic Activities of 3,5,3′-*L*-Triiodothyronine and *L*-Thyroxine in Myxedema. S. P. Asper Jr., H. A. Selenkow and C. A. Plamondon.—p. 164.

Local Use of Hydrocortisone Acetate.—According to Robinson, critical evaluation of the local use of hydrocortisone acetate (Compound F) has been hampered by the meager supply of ointment available for research purposes. The present communication deals with the results obtained in 42 patients. The 42 patients included 28 with atopic dermatitis, 8 with pruritus vulvae, 3 with pruritus ani, and 3 with discoid lupus erythematosus. The topical applications were made with an ointment containing 2.5% hydrocortisone acetate. Twenty of 28 patients with atopic dermatitis showed definite improvement within 24 hours. All patients had exacerbations w[illegible] applications were discontinued. Five of eight patients with pruritus vulvae and one of three patients with pruritus ani improved as long as the ointment was applied but experienced flare-ups on withdrawal. The results in discoid lupus erythematosus were such that further study is indicated, since other investigators do not agree as to its value.

Connecticut State Medical Journal, Hartford

17:809-892 (Oct.) 1953

What is Education? R. Livingstone.—p. 811.
Nutrition and Obesity Problem. R. J. Anderson.—p. 815.
Lymphosarcoma of Uterus: Report of Two Cases. L. L. Walton.—p. 819.
Statistical Study of Premature Infant. K. J. Edgar and M. Bogin. —p. 822.
Partial Agenesis of Corpus Callosum with Porencephaly. J. Greenblatt and C. Anderson.—p. 824.
Re-Education—Method of Psychiatric Rehabilitation. W. B. Terhune. —p. 828.
Beneficial Effect of Postpartum Plasma in Case of Myasthenia Gravis. L. W. Granierer.—p. 834.

Hawaii Medical Journal, Honolulu

13:1-88 (Sept.-Oct.) 1953. **Partial Index**

Human Infestation with Fasciola Gigantica. G. N. Stemmermann.—p. 19.
*Harada's Disease—Vogt-Koyanagi Syndrome: Diffuse Melanitis. H. E. Crawford.—p. 26.

Harada's Disease (Diffuse Melanitis).—Crawford illustrates with two case reports a rare entity with many bizarre aspects that seriously affects the eyes. The disease is characterized primarily by bilateral uveitis associated with retinal detachment. The distinction between Harada's disease and Vogt-Koyanagi syndrome depends on the location of the inflammation. In Harada's disease, which has a somewhat better prognosis, the inflammation is limited to the posterior segment; in the Vogt-Koyanagi syndrome, it extends to the ciliary body and iris and usually results in complete loss of vision. Both of these entities are associated with one or all of the following conditions that appear at varying periods after the onset of the disease: headache, meningismus, deafness, dizziness, alopecia, vitiligo, and poliosis. The cause is not known, but it occurs in moderately pigmented persons (Japanese and Italians). There are no reports of it having occurred in blond persons. The presenting symptom that brings the patient to the physician is loss of vision. This is rapid, progressive, and usually complete in the course of a week or two. It is frequently associated with headache. Dizziness and deafness appear about the second or third week. Alopecia, poliosis, and vitiligo are later developments. The prognosis is always grave, and there is as yet no treatment of demonstrated value. Foreign protein, tuberculin, diphtheria antitoxin, and uveal pigment injections, as well as a host of drugs, have been used to no avail. The second of the cases presented is noteworthy, because tissue removed at iridectomy could be examined, and treatment with cortisone proved of value during the early stages, but after a recrudescence of the disease it did not appear to have any particular effect. Its use should probably be continued for a long period to achieve a cure. It appears that the disease involves the pigment or melanin bearing tissues. There is melanin in the uveal tract, and the disease is most intense in the eye. There is melanin in the skin and in the hair. This accounts for the vitiligo and poliosis and presumably the disturbance of the pigment in the germinal layer of the hair follicle accounts for the loss of hair. A disturbance in the pigment granules in the cells of Hansen in the organ of Corti could explain the deafness, and involvement of the pigment granules in the hair cells of the utricle, saccule, and ampullae of the semicircular canals can account for the dizziness that sometimes occurs. Melanoblasts are found in the pia mater of the ventral surface of the medulla oblongata. The presence of meningismus with an increased cell count in the spinal fluid could be the result of involvement of this tissue. The essential factor of Harada's disease and of the Vogt-Koyanagi syndrome seems to be an inflammation of the melanin bearing tissues, either on an allergic or an infectious basis. The author feels that the term "diffuse melanitis" is preferable to the eponymic designations.

Iowa State Medical Society Journal, Des Moines

43:403-442 (Oct.) 1953

*Comparative Radiotherapeutic Results in Carcinoma of Cervix Uteri as Modified by Prior Surgery and Radiation. H. B. Hunt.—p. 403.
Pudendal Block Anesthesia in Obstetrics. J. R. Wilson and K. L. Cooper. —p. 409.
Pitfalls in Electrocardiography. D. J. Wagner.—p. 412.
Problems Posed by Newborn Infant of Diabetic Mother. R. D. Gauchat. —p. 416.

Comparative Radiotherapeutic Results in Carcinoma of Cervix Uteri.—Carcinoma of the cervix uteri is the commonest form of gynecologic cancer and the one that best lends itself to treatment. Recent improvements in treatment have been due to earlier diagnosis, better recognition of in situ lesions that are often not cancerous or, if they are, that do not usually lead to clinical carcinoma, surgery involving radical pelvic lymph node dissection as a preventive measure as well as total hysterectomy, more effective use of roentgen and radium therapy, and new developments in radiation therapy, such as ultrapenetrating megavolt roentgen and radiocobalt therapy, rotational irradiation, and experimental use of radioactive gold. Care must be exercised in the use of these methods, as shown by the present study. The absolute five year survival rate, with conventional radiotherapy in 318 cases of carcinoma of the cervix uteri unmodified by prior surgery or radiation treated at a state and a private hospital in Nebraska between 1937 and 1947, was 48.1% (state cases 43.1%; private cases 57.9%). Twenty-eight cases modified by prior surgery showed an over-all five year survival of 35.7%: stage 3 and 4 cases no survival, stage 2 cases 14% survival, and stage 1 cases 69.2% survival. These figures demonstrate that surgery prior to irradiation becomes increasingly deleterious with the advance of the disease. Twenty cases of carcinoma of the cervix modified by prior radiation therapy showed only one (5%) five year survival and with increased incidence of sequellae following reirradiation. Since reirradiation is ineffective and

hazardous, the initial application must be optimal in concept, distribution, and dosage. Any carcinoma of the cervix persistent or recurrent after surgery and controllable by radiotherapy could have been more assuredly and satisfactorily controlled by initial radiotherapy alone. Surgery should serve these purposes only: (1) identify undiagnosed cervical lesions —biopsy, (2) remove verified in situ carcinoma—total hysterectomy with removal of the vaginal cuff, (3) remove carcinoma of the cervix invading bladder or rectum but confined to the pelvis—partial or complete pelvic exenteration, (4) remove residual or recurrent carcinoma after near tolerance radiation—radical hysterectomy, and (5) palliate stage 4 cases with nerve plexus pain and edema—pelvic sympathectomy or cordotomy. The preferred primary treatment for clinical carcinoma of the cervix uteri is irradiation combining roentgen rays and radium.

Journal of Pediatrics, St. Louis

43:371-498 (Oct.) 1953

*Cat-Scratch Fever. C. W. Daeschner, G. W. Salmon and F. M. Heys. —p. 371.

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Gamma Globulin Dosage and Measles Control: Report of 188 Cases. L. Bivings.—p. 401.

Encephalitis in Children with Measles Who Were Given Attenuating Doses of Gamma Globulin. L. Odessky, A. V. Bedo, H. Weisler and B. Newman.—p. 404.

Extravesical Ureteral Ectopia. W. L. Huffman, L. Persky and J. J. Joelson.—p. 407.

Use of Mysoline in Treatment of Epilepsy. P. J. Doyle and S. Livingston. —p. 413.

Bronchial Adenoma. S. M. Berger, A. G. Boreadis and V. Kremens. —p. 417.

Allergenicity of Modified and Processed Foodstuffs: IV. Orange: Allergenicity of Orange Studied in Man. B. Ratner, S. Untracht, H. J. Malone and M. Retsina.—p. 421.

*Further Examples of Endocardial Cushion Defect in Production of Cardiac Anomaly Complex: Presentation of Three Cases from Autopsy Reports. A. W. McCullough.—p. 429.

Rehabilitation of Child with Numerous Congenital Defects. A. Kanof and S. Bernstein.—p. 434.

Bilateral Epididymal Tuberculosis in an Infant. C. A. Wattenberg, M. Abrams, H. K. Lewis and J. Lewis.—p. 443.

Neonatal Symmetrical Pedal Gangrene with Complete Recession. H. E. Stadler.—p. 447.

Surgically Acquired Hypothyroidism in Child with Coarctation of Aorta. E. E. Johnson and O. C. Bruton.—p. 449.

Roentgenographic Diagnosis of Coarctation of Aorta in Two-Day-Old Infant. D. N. Marks, R. S. Shapiro and L. G. Joseph.—p. 453.

Hypoplastic and Aplastic Anemias of Infancy and Childhood: With Consideration of Syndrome of Nonhemolytic Anemia of Newborn. C. H. Smith.—p. 457.

Cat Scratch Fever.—Twelve cases of cat scratch fever in children are reported from the south Texas area. These cases were seen within the past 18 months, which emphasizes the probable widespread incidence and frequent observation of this disease in the everyday practice of medicine. The patients exhibited the characteristic features of the disease, malaise, fever, and unexplained local adenopathy in which the size of the enlarged lymph nodes may be quite impressive. The incubation period varied from 10 to 30 days. The patients were in close association with cats, although specific instances of scratch could be elicited in only some of the patients. At the time medical advice was sought, significant enlargement of one or more lymph nodes was the chief presenting symptom. Both axillary and epitrochlear lymph nodes on one side were involved in two patients; epitrochlear or axillary involvement alone occurred in six. In four involvement was limited to the inguinal region. A typical primary lesion was identified definitely in only seven patients, and occasionally an exacerbation of redness and swelling was observed at the site where the primary lesion had been in the process of healing. A clearly positive skin reaction to intradermally injected Frei antigen prepared from the bubo of the first patient was observed in all patients within 1 to 14 months after the onset of lymphadenitis. By way of comparison, a group of control persons was tested with this antigen; this group consisted of normal volunteers, of patients with no evidence of lymph node disease, and patients with suppurative or nonsuppurative adenopathy thought to be attributable to other causes than cat scratch fever. The results of these skin tests were consistently negative. No untoward effects of any kind occurred as a result of the injection of the antigenic skin test materials. Skin test antigens then were prepared from material obtained by needle aspiration of involved lymph nodes in two additional patients. All three antigen samples gave similar results: positive skin reactions in the patients with cat scratch fever and negative reactions in controls, irrespective of the sample of antigen employed. No specific therapeutic measures were of definite benefit. Chlortetracycline (aureomycin) seemed to shorten the febrile course in some cases and to alleviate the systemic symptoms to some degree. While the etiology of this disease entity has not been clarified completely, there is considerable evidence in support of the view that the infectious agent belongs to the psittacosis-lymphogranuloma group of viruses.

Endocardial Cushion Defect.—A complex anomaly of the heart involving (1) patency of the interventricular septum in the region of the root of the great vessels and (2) transposition or other anomaly of the great vessels, external to the heart, was revealed by necropsy in a girl and a boy aged 14 months and 4 years at the time of death and in a male infant stillborn during the eighth month of pregnancy. The three cases described are examples, in varying degree, of failure or retardation of endocardial cushion development during the period from the fourth to the seventh week of gestation, i. e., the period of septation. It is a critical one in cardiogenesis because so many structures first appear and, also, the velocity of the developmental process is at a peak. The absence of endocardial cushion development in the case of the girl left the primitive atrioventricular orifice undivided; this in turn allowed a single column of blood to enter the ventricle and accordingly a single chamber, rather than two chambers with a septum between them, was formed. The absence of endocardial cushions left the bulb without impetus to ridging and septation, and a single aorticopulmonary trunk persisted. The undivided ventricle and undivided aorticopulmonary root served to supply the lungs, as all other portions of the body, with the required blood; hence there was no excess blood particularly sent to the lungs that could not be utilized by that developing system, and that explains the total absence in the girl of ductus arteriosus for which there was no need. The case of the stillborn was interpreted as an example of an early disturbance in endocardial cushion development that subsequently was erased by a more or less normal development. The transposition of the great vessels indicated that the endocardial cushion development was sufficiently delayed to disturb the normal ridging and septation of the bulb. The patency in the far anterior portion of the intraventricular septum likewise indicated that, although the bulbar septum and the interventricular septum formed, the ventral endocardial cushion failed to contribute at the appropriate time that material that would have united these two septums and would have actually completed septation of the ventricle and the bulb. The normal appearance of the valves and related structures showed that this early deficiency in development was later compensated. Enlargement of the heart to the right and a peculiar shallow cone-shaped depression on the left face of the interventricular septum at a point just inferior to the aortic root were observed in the case of the 4-year-old boy. Probing of this depression showed a canal-like continuity that penetrated the interventricular septum and emerged on the right side of the septum between two ridges of the trabeculae carneae. It is assumed that this channel had a valve-like action and that the channel allowed blood to pass from the left to the right side, thus accounting for the clinical history of heart murmur. The need for careful postmortem examination of specimens is emphasized particularly in cases in which a history or suggestion of cardiac or cardiovascular irregularity exists.

FOREIGN

Canadian Medical Association Journal, Montreal

69:349-468 (Oct.) 1953

A Century in Retrospect. H. L. Scammel.—p. 349.
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Digestive Symptoms in Angina Pectoris: Clinical Study. B. Carasso and J. Longtin.—p. 364.
Purpura Fulminans with Afibrinogenaemia. F. C. Heal and G. Kent. —p. 367.
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Post-Sanatorium Institution for Rehabilitation in Tuberculosis. B. McKone. —p. 395.
Observations on Sensitized Sheep Cell Haemagglutination Test for Tuberculosis. A. R. Armstrong and J. H. Lee.—p. 403.
Bronchogenic Carcinoma. N. Berkson.—p. 406.
Behaviour Problems in Children. P. Williamson.—p. 412.
Thoracoscopy as Diagnostic Procedure in Pulmonary Tuberculosis. Z. Gorecki.—p. 415.
Toxicity Studies on Some Newer Long-Acting Local Anaesthetics. M. O. Maykut and E. A. Ryan.—p. 419.
*Tumor Cells in Bone Marrow Smear. H. E. Amy and C. H. Jaimet. —p. 424.

Tumor Cells in Bone Marrow Smear.—Anemia, or abnormal white blood cell counts, or a high sedimentation rate, in conditions defying diagnosis by other means led the authors to do more exhaustive studies of bone marrow aspirates. Some years ago, they had noted tender areas in the sternum of patients with undetermined diagnosis. They observed extraneous cells in these smears and speculated that they might be metastases. Subsequently, they performed marrow punctures oftener and pressed for postmortem, biopsy, or radiographic confirmation of their tentative diagnosis of metastatic tumor. It was not until at least 50 marrow aspirates with these extraneous cells were observed that it was realized that many patients with carcinoma were being diagnosed first in the hematology laboratory by marrow studies, and subsequently the authors even felt able to a degree to correlate the morphology of the cell type found in the aspirate with the primary site of the tumor growth. From June, 1949, to June, 1952, a total of 1,100 marrow punctures were performed, and 335 of these were specifically examined for malignant cells; 265 yielded positive results. The majority were confirmed by surgery, radiography, biopsy, or postmortem examination, and, in 164 of the 265 patients, there had been no clue to the diagnosis prior to the marrow puncture. Cells that the authors regard as malignant proliferate through the marrow and cannot be identified as hemopoietic cells. They may cause a reaction in the hemopoietic cells in the form of a leukoerythroblastic response, or they may stimulate an increase in plasma cells. Furthermore, eosinophils increase only in the plasma, and not in the peripheral blood; this is suggestive of a response within the marow to foreign protein metabolites. Identification of the tumor cells is facilitated by their tendency to form a syncytium or group within the hemopoietic substance. They vary in size and behavior, depending on the organ in which the primary tumor is situated. They have one or two nucleoli, large in proportion to the nucleus, and the nucleus predominates in size as compared with the cytoplasm. The chromatin structure shows a loosely knit, coarse net of chromatin threads set against a colorless ground matrix. The cytoplasm is fragile, often shows a slight to deep basophilic reaction, and, at times, contains vacuoles. Although the hyaloplasm is often colorless, the spongioplasm may show a coarse, unevenly distributed granulation, acidophilic in its reaction and appearing more like a precipitation than a functional organization of the cytoplasm. This latter finding is particularly true in the cells from bronchogenic carcinoma. The authors comment further on the possible relation between cell type and site of primary tumor and then discuss reticulum cell and plasma cell. They feel that physicians generally have not been made aware of the diagnostic importance of bone marrow studies.

Deutsche medizinische Wochenschrift, Stuttgart

78:1355-1388 (Oct. 2) 1953. **Partial Index**

Surgical Treatment of Aseptic Bone Necroses. P. Pitzen.—p. 1355.
Rare Form of Leptospirosis. K. Marcuse and E. Eggert.—p. 1360.
Artificial Respiration. G. Fruhmann, B. Klun, H. Valentin and others. —p. 1365.
*Is Lipstick Harmful? H. Ruther and H. C. Friederich.—p. 1370.
Excretion of 17-Ketosteroids and of Corticoids in Chronic Liver Diseases During Tolerance Test with Corticotropin. K. P. Eymer and H. Moll. —p. 1376.

Is Lipstick Harmful?—The case reported by Ruther and Friederich describes a woman, aged 32, who three days before used the lipstick of another person, who had purchased it three years previously, but had used it rarely. In the evening of the day the lipstick had been applied, the lips became red and swollen and there was severe pruritus in the perioral region. On the next morning, when application of powder brought no relief, the patient consulted the authors who found that both lips and the adjoining portion of the skin were edematous. Numerous blisters ranging from pinpoint to pinhead size were distributed over the edematous area. Some of the blisters had ruptured and weeping resulted. There were also rhagades. The submandibular lymph nodes were enlarged and sensitive to pressure. With moist applications of distilled water, the symptoms subsided in two days. Epicutaneous tests with the lipstick material resulted in positive reactions. Control tests with the same lipstick material in 20 other persons yielded positive reactions in 2. In view of the widespread use of lipsticks, harmful reactions are extremely rare, and if they do occur they are often the result of hypersensitivity to eosin or more rarely to eosinic acids. The photosensitization ascribed to eosin is, in some of the cases, probably the result of a summation of irritations in the naturally ray-sensitive region of the lips. Today not eosin but eosinic acids are used in the preparation of lipsticks, and, if the presence of castor oil can be ruled out, there is practically never a reaction of hypersensitivity. At any rate, inflammation of the lips after the use of lipstick is not necessarily the result of hypersensitivity to eosin; the constituents of the lipsticks should be investigated whenever there is an undesirable reaction. Rancidity resulting from long storage of the lipstick may also cause reactions of intolerance. Finally, the summation of subthreshold irritation by the coloring matter and the lipstick base may cause a reaction. As to the cancerogenic effect of the dyes contained in the lipstick, the authors have never seen a case in which the development of carcinoma could be traced to the use of lipstick.

Lancet, London

2:685-738 (Oct. 3) 1953

Overnutrition and Undernutrition: I. Causes. R. A. McCance.—p. 685.
*Treatment of Tuberculous Meningitis with Isoniazid. T. Anderson, M. R. Kerr and J. B. Landsmann.—p. 691.
Treatment of Tuberculous Meningitis with Streptomycin and Isoniazid. J. Torres-Gost.—p. 693.
C.S.F.—Isoniazid Levels in Tuberculous Meningitis. A. P. Fletcher. —p. 694.
Anaemia Associated with Haemophilus influenzae Meningitis. J. Schiavone and S. D. Rubbo.—p. 696.
*Lactosuria and Glycosuria in Pregnancy and the Puerperium. F. V. Flynn, C. Harper and P. de Mayo.—p. 698.
Impalement of the Rectum. L. P. Thomas.—p. 704.
Exercise Tests During Treatment of Hypertension with Hexamethonium. V. Rønnov-Jessen.—p. 706.
Respiration Pump for Poliomyelitis. W. R. Russel and E. Schuster. —p. 707.

Treatment of Tuberculous Meningitis with Isoniazid.—Seven patients with tuberculous meningitis were given both streptomycin and isoniazid during the first week of treatment, but afterwards streptomycin was discontinued and the treatment carried out with 10 mg. of isoniazid per kilogram of body weight given orally each day. A second group of seven patients with tuberculous meningitis treated with streptomycin alone was used as a control, with similar patients from each group matched as pairs. The initial fever of the patient treated with isoniazid in each pair disappeared as soon as, but oftener sooner than, that of the patient treated with streptomycin. The levels of the cells, protein, sugar, and chlorides of the cerebrospinal fluid returned to normal more rapidly in the patient of each

pair treated with isoniazid, almost without exception. The patients treated with isoniazid were happier and more comfortable because they did not have to undergo the tedious intramuscular and intrathecal injections necessitated by streptomycin therapy; it is believed that these injections are also responsible for the more extensive disturbances in the cerebrospinal fluid experienced by the patients treated with streptomycin alone. The appetite of patients given isoniazid improved, and there was an obvious gain in weight. Follow-up of these patients has not been long enough to judge the results completely, but it would appear that isoniazid alone has been effective in the treatment of tuberculous meningitis and that the method warrants further investigation. The authors do not suggest that isoniazid alone be regarded as adequate therapy for patients with tuberculous meningitis, because of the rapidity with which tubercle bacilli may develop resistance to isoniazid alone.

Lactosuria and Glycosuria in Pregnancy and the Puerperium.—Past reports on glycosuria and lactosuria in pregnancy showed considerable variance. It was generally believed that, although glycosuria frequently occurred during pregnancy, lactosuria was not found during pregnancy but only during the puerperium. The present study is based on urine specimens from 2,372 prenatal patients, 656 postnatal patients, 240 nonpregnant women, and 132 men, analyzed by qualitative Benedict tests and by paper partition chromatography. It was found that lactosuria is common during pregnancy, occurring about twice as often as glycosuria. Lactose, usually in small amounts, was found in 51% of all prenatal patients, being detected at some time in 94% of patients regularly attending the prenatal clinic of the University College Hospital in London. Glucose was found in 24% of prenatal patients, but 33% of the regular patients never excreted detectable quantities. Prenatal lactosuria increases in incidence as pregnancy advances, was found oftener in the afternoon, and more commonly in primigravida women. Prenatal glycosuria was found oftener in the afternoon and more frequently in older patients. The frequent excretion of considerable quantities of lactose during the puerperium is confirmed; and pregnancy glycosuria was found to disappear rapidly after delivery. Lactosuria occurs in men as well as nonpregnant women eating a normal diet. Lactose, usually a trace, was detected in the urine of 9% of these patients; it is probably alimentary in origin. In pregnancy, glycosuria is probably due to a low renal threshold for glucose and lactosuria to escape of lactose formed in the mammary glands.

2:739-788 (Oct. 10) 1953

Overnutrition and Undernutrition: II. Effects. R. A. McCance.—p. 739.
Transfusion by Intra-Arterial Route. A. S. Brown.—p. 745.
*Hyaline Membrane in Neonatal Lung. A. E. Claireaux.—p. 749.
Gastric Resection for Gastroduodenal Hemorrhage Without Obvious Ulcer. G. Ferguson.—p. 753.
*Controlled Hypotension with Arfonad in Neurosurgery with Special Reference to Vascular Lesions. S. Anderson and W. McKissock.—p. 754.
Results of Treatment of Infantile Cerebral Palsy. E. Collis.—p. 757.
Effects of Inhalation of Sulphur Dioxide by Man. M. Amdur, W. W. Melvin Jr. and P. Drinker.—p. 758.
Polycythaemia with Fibroids. A. P. Thompson and F. G. W. Marson.—p. 759.

Hyaline Membrane in the Neonatal Lung.—Out of 810 necropsies on stillbirths and neonatal deaths, 108 cases of hyaline membrane were found. It was then noted that none of the infants in which it occurred had been stillborn; the membrane developed in 108 (29%) of 376 liveborn infants. Hyaline membrane was the only abnormality in 81 cases (75%). Twenty-two of the 108 infants were delivered by cesarean section; 18 of the 104 pregnancies were twin ones; and there was one triplet in the series. It is suggested that the hyaline membrane, which is never present before birth, is formed from squames in the liquor amnii. The liquor is aspirated into the fetal lung and the squames undergo progressive hyalinization and fusion. This phenomenon occurs mainly in premature infants and infants born of mothers with some abnormality in pregnancy that renders the infant less able to cope with aspirated liquor amnii. The atelectasis associated with hyaline membrane in the newborn is partly the result of direct obstruction of the airways by plugs of hyaline material and partly the result of air being trapped in the distal air sacs when the alveolar ducts are sealed by membrane. Suitably treated deposit from human liquor amnii, when injected tracheally into the rat, will produce a hyaline membrane in the animal's lung.

Controlled Hypotension with Arfonad in Neurosurgery.—In fifty-two patients on whom major craniotomies were performed since March, 1953, at St. George's Hospital, London, hypotension was induced by Arfonad (*d*-3,4[1′,3′-dibenzyl-2′-ketoimidazolido]-1, 2-trimethylene thiophanium *d*-camphor sulfonate) during the operations. Four patients died; three of these were very poor subjects for major surgery. There was no reason to believe that induced hypotension influenced these fatalities. All patients to whom Arfonad was administered had a fall in blood pressure; in only one instance was there a failure to lower the blood pressure to the level requested by the surgeon. After the blood pressure had fallen, the hypotensive state was easily maintained; in only two cases was it necessary to supplement the drug with procaine amide hydrochloride. Although Arfonad is short-acting, the blood pressure was seldom restored as soon as the infusion was stopped; there was usually a lapse of from 1 to 20 minutes. This disadvantage, with two exceptions, was overcome by flattening the table. In two cases methamphetamine (Methedrine) was injected to hasten the return to normal blood pressure. Arfonad is superior to the methonium compounds for inducing hypotension, especially in cerebrovascular surgery in which hypotension is essential, because it is short-acting, gives the anesthetist greater control of the blood pressure, but still reduces the hemorrhage and intracranial tension to the satisfaction of the surgeon. It must be emphasized, however, that Arfonad is not an answer to the dangers of hypotension itself and that it should be used only in selected cases in which that risk is necessary to reduce the greater risk of the operation.

Medical Journal of Australia, Sydney

2:321-360 (Aug. 29) 1953

Pattern of Renal Response to Circulatory Stress. E. G. McQueen, M. P. Summerfield and E. Trewin.—p. 323.
Calorimetry: Method of Estimating Peripheral Blood Flow. A. J. Barnett and G. R. Wigley.—p. 326.
Vaginal Delivery Following Caesarean Section. J. Nattrass.—p. 329.
Serum Protein Levels in Normal Nonpregnant and Pregnant Women. B. Liddelow.—p. 332.

2:361-400 (Sept. 5) 1953

Vertigo. R. G. Mackay.—p. 361.
Vertigo. C. B. Hudson.—p. 363.
Isonicotinic Acid Hydrazide in Pulmonary Tuberculosis. R. M. Ford.—p. 366.
Value of Liver Biopsy in Diagnosis of Tuberculosis and Sarcoidosis. E. S. Finckh, S. J. Baker and M. M. P. Ryan.—p. 369.
Source of Tuberculous Infection in Patients of Royal Alexandra Hospital for Children. R. M. Mills.—p. 374.
General Anaesthesia for Dentistry: Hazardous Field of Practice. R. B. Speirs.—p. 376.

Minerva Ginecologica, Turin

*Effects of Chorionic Gonadotropin in Female During Old Age and Problem of Sexual Endocrine Activity of Adrenal Cortex. E. Moracci.—p. 421.
Treatment of Anuria. P. Quaini.—p. 429.
Accidental Injection of Contrast Medium into Vessels During Hysterosalpingography. A. Tetti.—p. 439.
Study of Ureteral Peristalsis with Ureterotonographic Investigation. P. Quaini.—p. 445.

Chorionic Gonadotropin in Aged Women.—The effects of chorionic gonadotropin on the urinary excretion of the estrogens and the 17-ketosteroids were studied in 10 women, 2 to 34 years after menopause. The women, 49 to 78 years of age, were all well. The estrogen and 17-ketosteroid levels were determined before and 24, 48, and 72 hours after the hormone was administered. Estrogens were not found in the urine of some women before the treatment, and in the others the level varied from 10 to 21 gamma per liter of urine. The 17-ketosteroids were found in quantities that were in inverse ratio to the person's age. One intramuscular dose of 2,500 I. U. of chorionic gonadotropin was tolerated well. Estrogens appeared in the urine of the women in whom they had not been found before treatment, and they increased markedly in the others. The increase was more pronounced after 24 hours, and there was a return to the initial values

after 72 hours. The increase in the level of 17-ketosteroids was less pronounced and reached its highest value after 72 hours. These changes in the urinary excretion of the estrogens and the 17-ketosteroids are ascribed to the reaction of the adrenal cortex to the stimulus of the chorionic gonadotropin. They seem to indicate that the reticular zone of the adrenal cortex elaborates not only the 17-ketosteroids but also the estrogens. The functional correlations between the adrenal cortex and the anterior lobe of the hypophysis in women of this age group who have, as a rule, ovary deficiency need to be studied. The mechanism of action of the endocrine activity of the adrenal cortex in them may then be explained. The administration of chorionic gonadotropin to the author's patients showed biological conditions that could not be compared with the natural conditions because the hormone used was of chorionic origin and also because large doses of it were used.

Minerva Medica, Turin

44:585-612 (Sept. 12) 1953

*Value of Cytological Examination of Sputum of Persons with Primary Malignant Tumor of Lung. L. Bussi and L. Manzocchi.—p. 585.
Behavior of "In Vitro" Heparin Tolerance Test with Reference to Tests of Plasma Coagulation. G. Crolle, F. Boglione and S. Bianco.—p. 587.
Study of Venous Thromboses. R. Martino.—p. 594.
Cardiorheumatic Center for Diagnosis and Control of Rheumatism in Children: Its Importance. C. Imperato.—p. 602.

Primary Cancer of Lung and Cytological Study of Sputum.—The authors establish a diagnosis of primary malignant tumor of the lung only after they have made repeated studies of the patient's sputum with the May Grünwald-Giemsa staining method. This procedure is a valuable diagnostic means in the hands of experienced persons and is easy to perform. The morphological and staining characteristics of the nuclei and cytoplasm can be seen simultaneously. The diagnosis of primary malignant tumor of the lung is easily established when the nucleus is markedly hyperchromatic and dark maroon, its chromatin is irregularly clumped with one or more nucleoli varying in shape and size and stained in light blue, and the cytoplasm is dark blue. When these atypical characteristics are not present, the diagnosis is established on the basis of (1) increased cell volume (the macrophages are easily excluded), (2) polymorphism and marked cellular and nuclear anisocytosis, (3) enlarged nuclei, and (4) prevailing nuclear hyperchromatism, chromatic irregularities, one of more nucleoli, and basophilic cytoplasm. Sometimes this method makes possible the histological diagnosis of the cancer. The authors report on 100 persons in whom the presence of a primary malignant tumor of the lung was suspected. They used this method and obtained positive results for cancer in 87. Surgical exploration, endoscopic biopsy, or the clinical course confirmed its presence in all of the patients. They ascribe the false negative results to errors in the procedure and also to the fact that only a few smears could be studied for each patient. The diagnosis should be established only after numerous sputum smears of each patient have been studied. Repeated negative results in the same patient, when the smear is made and studied by competent and experienced persons, almost always indicate that a primary malignant tumor of the lung is not present.

Presse Médicale, Paris

61:1247-1266 (Oct. 3) 1953

Saturnism from Water: Caused by Ground Wire of Radio Set. H. Desoille and C. Albahary.—p. 1247.
*Place of Somatotrophine (STH) in Methods of Hibernation Therapy. H. Laborit, R. Favre, J. Dechen and G. Bastit.—p. 1249.
Therapeutic Use of Ester Alkaloids from White Hellebore in Treatment of Arterial Hypertension. J.-A. Salva and F.-L. Tarrida.—p. 1251.

Somatotrophine (STH) in Hibernation Therapy.—Somatotrophine (STH) is the name given to a somatotropic pituitary extract that was first developed in conjunction with a new method of psychotherapy—prolonged sleep therapy that relaxes the autonomic nervous system by means of pharmacodynamic agents. Somatotrophine now appears to be of value in artificial hibernation for surgery as well. In studying animals that hibernate naturally, it was found that the involution of their endocrine systems during hibernation is only partial; protein anabolism is possible, and there is endocrine hyperfunction of the pancreas. Since the injection of STH in man promotes protein anabolism, prevents the using up of sugars, and causes mobilization and catabolization of fats, while requiring the presence of insulin to offset the protein anabolism, it was hypothesized that this substance is the vital one for the prevention of hyperglycemia in hibernating animals and that it could be used to improve existing methods of artificial hibernation that had always brought about hyperglycemia. When STH was used in addition to cold, it enabled the authors to prolong the state of artificial hibernation in man without fear that metabolic disorders would persist after the return to normal temperature.

61:1267-1286 (Oct. 7) 1953

Histaminopexic Power of Blood Serum: Its Absence in Allergic Patients. J.-L. Parrot and C. Laborde.—p. 1267.
*Streptomycin in Intravenous Infusion: Results of 100 Cures and 5,000 Infusions. Y. Hebraud, M. Bertrac and P. Maufoy.—p. 1269.
Actinomycin C and Its Antitumoral Action. A. Ravina.—p. 1270.

Streptomycin in Intravenous Infusion.—Results of the treatment of 100 tuberculous patients with streptomycin in intravenous infusions, accompanied by *p*-aminosalicylic acid and, later, isoniazid have been excellent and have demonstrated the superiority of the intravenous to the intramuscular route. The patients, who were all cured, were treated in the course of the past two years by means of one three hour continuous slow infusion a day of streptomycin dissolved either in *p*-aminosalicylic acid or in a physiological serum, the *p*-aminosalicylic acid being administered orally. The total number of infusions given was 5,000; 4,616 of the first type described were given to 95 patients and 384 of the second type to 5 patients. Isoniazid was added to the last 1,300 infusions of all the patients; cures were effected in from 30 to 148 days. Tolerance of the streptomycin was good; the usual reaction to infusion of *p*-aminosalicylic acid appeared in some patients, but it is noteworthy that there were no such side-effects in the five patients to whom it was given orally. There were no vestibular or cochlear disturbances. No more resistance developed than does when streptomycin is administered intramuscularly. The infusion method has proved effective in different forms of pulmonary tuberculosis and in several cases of extrapulmonary tuberculosis, notably tuberculous meningitis.

61:1287-1304 (Oct. 10) 1953

*Study of Cutaneous Circulation in Permanent Arterial Hypertension. A. Lemaire, J. Loeper and E. Housset.—p. 1287.
Invasion of Lymph Nodes in Carcinoma of Cervix Uteri: Consequences for Therapy. A. Tailhefer.—p. 1289.
Research on Synthetic Sympathicolytic and Oxytocic Substances from Ergotamine Series. E. Savini.—p. 1291.

Cutaneous Circulation in Arterial Hypertension.—Of the numerous suggestions advanced concerning the physiopathological mechanism responsible for permanent arterial hypertension, the one mentioned most frequently ascribes the condition to an increase in peripheral resistance combined with a permanent reduction in the lumens of the arterioles. This idea is supported by the fact that during the disease the cardiac output, venous pressure, and blood volume and viscosity remain normal or nearly so. Plethysmograms, sphygmograms, and measurements of arteriolar pressure were made on the digital pulps of 89 hypertensive patients and 92 normal controls. The authors conclude that in patients with arterial hypertension the cutaneous circulation does not necessarily play a part in the maintenance of the condition; hypertension may be contained within elastic arteries. When the cutaneous circulation is involved, it either increases the peripheral resistance—not at the level of the arteriole, but probably at the level of the metarteriole—or is affected by a true hyperkinesia in the vascular wall that contributes to the rise in maximal pressure. It is felt that the theory that blood vessels play only a passive role in blood circulation should be abandoned and that the notion of actual movement of the vascular wall should be applied to the problem of the physiopathology of the vascular muscle and of its basic sensitivity.

Riforma Medica, Naples

67:1017-1044 (Sept. 12) 1953

Treatment of Sepsis Due to Escherichia Coli. G. Suardi.—p. 1017.
*Isoniazid in Tuberculous Meningoencephalitis with Respect to Route of Administration and Its Concentration in Cerebrospinal Fluid. I. Ragno, P. Preziosi and G. Porcellati.—p. 1022.
Clinical and Experimental Study of Tissue Therapy. L. Pasquali and G. Arpesella.—p. 1027.

Isoniazid and Glutamic Acid in Tuberculous Meningoencephalitis.—The effects of oral, parenteral, intramuscular, and intravenous administration of isoniazid to patients with tuberculous meningoencephalitis and the concentration of the drug in the cerebrospinal fluid were studied. Massive doses of isoniazid (20 to 30 mg. per kilogram of body weight) gave good results when given orally. But, as a rule, large doses of the drug cause pronounced toxic effects of the nervous system. Since these side-effects are ascribed to the liberation of ammonia from the isoniazid molecule and since glutamic acid combines easily with ammonia to form glutamine, the authors studied the effects of simultaneous oral administration of isoniazid and glutamic acid in patients with tuberculous meningitis. Some patients were given the drug in regular doses (4 mg. per kilogram of body weight) with glutamic acid in the ratio of 10 parts to 1 part of isoniazid, and some were given the same dose without glutamic acid. Others were given massive doses of isoniazid (from 8 to 25 mg. per kilogram of body weight) without and with glutamic acid in the same ratio. There were no toxic disturbances in these patients, and the gastric tolerance was good. The spinal fluid concentrations of isoniazid were determined four hours after the administration of the drug. The levels of isoniazid in the spinal fluid of the patients who received massive doses of it with glutamic acid were far greater than those in the fluid of patients who were given the usual therapeutic doses with and without glutamic acid. The concentrations in these patients were bacteriostatic and may have been bactericidal. A concentration of 7.8 mcg. per cubic centimeter of fluid was found in one patient, and this is the highest concentration of isoniazid in spinal fluid so far reported in the literature. Although the various levels depended on physiological and pathological factors, there was always a certain ratio between the isoniazid concentration and the amount of drug administered. The authors conclude that treatment of tuberculous meningoencephalitis with large doses of isoniazid may be carried out on a large scale and with good results if the drug is administered orally with glutamic acid and with or without streptomycin.

Rivista d'Ostet. e Ginec. Pratica, Milan

35:329-392 (July) 1953. **Partial Index**

The Correct Use of Antibiotics. G. Nicora.—p. 329.
Liver Function in Pregnancy: Influence of Trigonelline Amide (N_1 Methylnicotamide Chloride) on Blood Level of Pyruvic Acid, Lactic Acid, and Amino Acids in Pregnant Women with Signs of Liver Insufficiency. G. Bartolomei and M. Rossi.—p. 336.
*Fetal Anasarca Due to Rh-Isoimmunization. G. Orlandini.—p. 348.

Fetal Anasarca.—A 30-year-old woman, eight months pregnant, sought help to interrupt a series of unfortunate pregnancies. Her first child was living and in good health. Her second child who was born apparently healthy died of severe icterus after three days. The third pregnancy resulted in a stillbirth and the fourth in an abortion during the eighth month of gestation. The patient was well; the general and obstetric examination revealed no abnormalities. The fetal heart beat was heard. She, her husband, and her daughter belonged to the same blood group. But at 37 C the patient's serum agglutinated the red blood cells of her husband and daughter. Complete anti-Rh antibodies were not found, but incomplete anti-Rh antibodies were present in the ratio of 1:64. The patient was kept under observation, and the pregnancy was to be interrupted at the end of the eighth month. Suddenly, a few days later, labor began, and a dead fetus, which weighed 2,800 gm., was delivered. The puerperium was normal. The anatomic findings revealed a state of anasarca and an enlarged liver and spleen. The histological study revealed severe cytological alterations that at some points were almost necrotic. These were ascribed to an antigen-antibody reaction in the tissues of the fetus. Some authors have found that in many fetuses the incompatible Rh antigen is found not only in the blood but also in many tissues, and their presence is responsible for the various clinical pictures of the hemolytic disease. Grünwald explained fetal anasarca as the effect of an anaphylactic shock caused in the fetus by the maternal antibodies. Since capillary permeability is a characteristic of shock, unlimited quantities of fluid may pass into the tissues and cavities of the fetus. The quantity and quality of the fetal antigens that enter the maternal blood stream and of the relative antibodies that pass through the placenta as well as the time in which the passage occurs are important factors. Since the placenta seems to become permeable to the maternal antibodies during the last months of gestation, attempts have been made to prevent or attenuate the damages of Rh-isoimmunization by interrupting the pregnancy early and treating the child with exchange transfusion. The author obtained good results in 10 instances.

Riv. di Pat. e Clin. della Tuberc., Bologna

26:193-256 (July-Aug.) 1953. **Partial Index**

*Clinically Primary Mediastinal and Pulmonary Localizations of Besnier-Boeck-Schaumann Disease. E. Fasano.—p. 193.
Intestinal Tuberculosis in Infancy and Adolescence and Influence of Antibiotic Therapy. E. Filla and E. Palumbo.—p. 211.
Therapeutic Effects of Surgical Extrapleural Pneumothorax Complicated by Reduction or Elision of the Extrapleural Cavity. M. Busin and O. De Lorenzi.—p. 223.

Besnier-Boeck-Schaumann Disease.—The cause of the Besnier-Boeck-Schaumann disease, or sarcoidosis, is still obscure. A skin manifestation is not always the first or a constant sign of the disease. It may involve the respiratory apparatus and lymph nodes and often the phalanges of the hands and feet, the nose, pharynx, spleen, liver, and nervous system. Lesions to the hilus and lungs are the commonest, and they are often confused with those of other pulmonary disease, especially tuberculosis. Lesions to the mediastinum and lungs are generally asymptomatic or present mild signs that are not characteristic (loss of weight, asthenia, elevated temperature, cough, dyspnea, and cyanosis). A great discrepancy between the physical and roentgenologic findings is characteristic of the disease. Roentgenography may present one of three pictures: involvement of the mediastinal lymph nodes with symmetric enlargement of the lymph nodes of the hilus; involvement of the lung; and involvement of the mediastinum and lungs. The diagnosis of sarcoidosis is based on clinical, roentgenologic, and laboratory data and histological findings of the bronchial mucosa obtained endoscopically. Differential diagnosis between a clinically primary pulmonary form of sarcoidosis and some forms of pulmonary tuberculosis is difficult. Many cases of sarcoidosis have been described in which the reaction to intradermal injection of tuberculin was positive. Some authors have reported that vaccination with BCG does not give rise to the reactivity to tuberculin in patients with this disease, and that an epithelioid reaction similar to that of sarcoidosis appears at the site of the inoculation. The disease may remain stationary for many years, and the patient may die from respiratory and cardiac insufficiency of the right side. Sarcoidosis is believed to be of infectious origin, but further studies are needed for a definitive statement. At present, on the basis of the anatomicohistological findings the disease is classified among those of the reticuloendothelial group. The author reports on two patients with sarcoidosis. In the first, a 53-year-old man, the disease involved the lymph nodes of the hilus and the diagnosis was established after two superficial lymph nodes were felt on the right side of the neck. The histological findings confirmed the diagnosis. In the second patient, a 35-year-old man, the disease involved the lungs. Diagnosis was established on the basis of the clinical, radiologic, and laboratory data. It was confirmed by biopsy of the bronchial mucosa and the histological findings of a lymph node that was felt under the right clavicle.

Semaine des Hôpitaux de Paris

29:2889-2940 (Oct. 2) 1953

*Results of and Remarks on Experimental Rapid Treatment of Early Syphilis with Penicillin. P. de Graciansky and C. Grupper.—p. 2889.
Effect of Primosecondary Syphilis on Liver as Studied by Functional Tests and Punch Biopsy of Liver. P. de Graciansky and J. P. Hardouin —p. 2904.
Syphilophobia. P. de Graciansky and E. Stern.—p. 2911.

Experimental Rapid Treatment of Early Syphilis with Penicillin.—Three things have revolutionized the treatment of syphilis: advances in serology, such as Nelson and Mayer's test, that permit better diagnosis; penicillin therapy; and discoveries in the bacteriology of the Treponema pallidum that have shown what is the most effective timing in the administration of penicillin. A detailed study was carried out by the authors and their colleagues of 53 patients treated with penicillin in the early stages of syphilis. There were three groups of patients: 10 in the preserologic stage of primary syphilis, 15 in the serologic stage of primary syphilis, and 28 in the early stage of secondary syphilis. Each patient received three intramuscular injections seven days apart; the first was of 3,000,000 units and the others of 1,500,000 or 3,000,000 units each, depending on the patient. The following results were noted: 1. Clinical symptoms definitely disappeared in all patients. 2. Treponema disappeared from the lesions within 24 hours after the first injection. 3. Tests of the serum were not positive after treatment in patients whose serum reactions had been negative before treatment; their cerebrospinal fluid also remained normal. Negative response or decrease in rate of reaction was obtained in patients whose serum gave a positive reaction before treatment. 4. Quantitative amelioration in the serum appears considerably sooner than qualitative amelioration and thus constitutes a better sign to be watched during treatment. 5. Before treatment, results of Nelson's test were positive in only the patients with a high rate of reaction; after treatment, negative responses were obtained in patients who had been treated early in the disease, but results of the Nelson reaction of patients treated late in the disease were not influenced. 6. None of the persons who had sexual relations with the patients treated showed any signs of syphilis nor did the children born of these patients. 7. The side-effects of therapy were insignificant. No precautions were sufficient to prevent the appearance of a Herxheimer reaction in 50% of the patients, but preventive therapy with cortisone (100 mg. of cortisone daily for five days) reduced this to an inconsequential level. The reaction may appear after any of the three injections. 8. Although the amount of penicillin in the blood varied unpredictably in each patient, these differences did not influence the results of therapy in any way. 9. The authors are of the opinion that their therapy was actually more extensive than is necessary for early syphilis; they plan to experiment with the use of one injection only. A report on this is forthcoming.

Settimana Medica, Florence

41:339-366 (Aug. 15) 1953. **Partial Index**

Experimental Studies on Reproductive Processes of Normal and Abnormal Bone Marrow: Proliferative Activity of the Hemocytoblast of Acute Leukosis. G. Astaldi and G. Mauri.—p. 339.
Brill-Symmer's Disease? Clinical and Morphological Considerations on a Case of Follicular Lymphoblastoma. M. Del Dotto and A. Torrini. —p. 345.
*Stellate Ganglion Block in Treatment of Hemiplegia Secondary to Cerebral Thrombosis and Embolism. U. Principe.—p. 352.

Stellate Ganglion Block in Hemiplegia Secondary to Cerebral Thrombosis and Embolism.—Patients with hemiplegia secondary to cerebral thrombosis or cerebral embolism are treated at the University of Florence surgical clinic with block of the stellate ganglion on the side opposite that involved by the paralysis. The anterior approach of Leriche or the posterior paravertebral approach of Mandl is used. The latter is preferred, since there is less danger of puncturing the subclavian artery, the rami of the brachial plexus, or the pleura. As a rule, one 20 cc. injection of a 1% solution of procaine hydrochloride without epinephrine is given every day. But, if the first injection causes a pronounced drop in the blood pressure, the ganglion is blocked every other day. A successful injection is followed by the onset of Horner's syndrome; if this does not develop, another injection is given within 20 minutes. The best results are obtained in young patients in whom the treatment is instituted as soon as possible after the stroke occurs. The author gave more than 300 injections to 18 persons with hemiplegia. This was secondary to cerebral thrombosis in 14 aged patients and to cerebral embolism in 4 patients with heart disease. Each patient was given from 10 to 30 injections; there were no untoward effects. The results evaluated 10 days after the last injection were good in six patients who made a complete recovery, fair in eight who recovered partially, and poor in four patients. Treatment was instituted too late in these patients, and their condition remained unchanged. The author never uses this treatment for patients in whom the stroke is caused by a cerebral hemorrhage. The vasodilatation that follows the interruption of the sympathetic innervation may contribute to increase the hemorrhage and thus aggravate the state of coma and the paralysis.

Thorax, London

8:167-250 (Sept.) 1953

Ulcero-Caseous Tuberculous Bronchitis: Method of "Spread" in Pulmonary Tuberculosis. J. W. Clegg.—p. 167.
Fibroma of Visceral Pleura. C. P. Thomas and C. E. Drew.—p. 180.
Surgical Anatomy of Pulmonary Vessels. J. C. Van der Spuy.—p. 189.
Fatal Bronchial Asthma: Series of 15 Cases with Review of Literature. B. V. Earle.—p. 195.
*Clinical and Pathological Study of Fatal Cases of Status Asthmaticus. J. C. Houston, S. De Navasquez and J. R. Trounce.—p. 207.
Conservative Thoracoplasty with Extrafascial Refills. R. Y. Keers and F. J. Sambrook Gowar.—p. 214.
Results of Collapse and Conservative Therapy in Pulmonary Tuberculosis. A. F. Foster-Carter, M. Myers, D. L. H. Goddard and others.—p. 221.
Consolidation in Primary Pulmonary Tuberculosis. D. Adler and W. F. Richards.—p. 223.

Fatal Status Asthmaticus.—The clinical and pathological features are described of eight women and one man between the ages of 26 and 64 who died in status asthmaticus but who did not show any evidence of respiratory infection or pulmonary heart disease. Asthma developed in all in adult life, and in five the age of onset was 40 or over. Seven of the nine patients had had asthma for eight years or less at the time of death; a rather short history was a common factor in other cases collected from the literature. It thus appears that death in status asthmaticus occurs particularly in adult life and may occur in patients in whom asthma is of quite recent onset. The gross morbid appearance of the lungs of the authors' patients conformed to previous descriptions, namely dry, emphysematous lungs with widespread bronchial obstruction by mucus. Microscopically, extensive detachment of the ciliated epithelium was observed in all cases examined. As ciliary activity is by far the most important mechanism by which mucus is normally removed from the smaller bronchi, loss of the ciliated epithelium seems to be the most probable explanation for the accumulation of mucus and bronchial obstruction. The longer the attack of asthma, the greater is the loss of ciliated epithelium, and a stage may be reached at which mucus can no longer be removed from the smaller bronchi. Clinically this stage is characterized by failure of the asthma to respond to antispasmodics. The authors believe that this is the mechanism in status asthmaticus that proves fatal. Most of the patients with a clinical diagnosis of status asthmaticus recover, and presumably in these patients there is only partial bronchial plugging with added bronchial spasm that in time becomes amenable to treatment.

Tubercle, London

34:233-258 (Sept.) 1953

Modern Concept of Pulmonary Collapse: Study in Functional Pathology. E. G. W. Hoffstaedt.—p. 234.
Further Thoughts on Silicosis. P. Heffernan.—p. 246.
Menstrual Characteristics of Tuberculous Women. G. R. Wadsworth. —p. 249.
Tuberculosis Yesterday and Today. G. L. Cox and H. F. Hughes.—p. 251.

BOOK REVIEWS

Surgery of Trauma. Edited by Warner F. Bowers, Colonel, MC, U.S.A. With forewords by Melvin A. Casberg, M.D., Chairman, Armed Forces Medical Policy Council, and Surgeons General of Army, Navy, and Air Force. Cloth. $15. Pp. 605, with 284 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

The author and 41 other contributors have produced a book that should be issued to every medical officer entering the military service. Furthermore, the book may serve as a reference for practicing physicians, who deal with trauma in civil life. The subject matter is presented in a concise and well-documented manner. The bibliography is extensive. The illustrations are well chosen and properly placed. The book is divided into sections on (1) the physiological aspects of the management of trauma, (2) regional wound surgery, (3) military considerations in wound management, and (4) study methods and research problems. Sections 2 and 3 are discussions of trauma as encountered in military surgery. The punch press type of trauma, so common in civil life, and diaphragmatic hernia caused by indirect trauma are not covered. One would expect the latter to be included in a book on the surgery of trauma, especially in our mechanized era when persons are more subject to indirect trauma, which can produce a tear in the diaphragm. Since the book deals almost exclusively with the trauma of war wounds, it is wrongly titled.

Textbook of Gynecology. By John I. Brewer, B.S., M.D., Ph.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School, Chicago. Cloth. $10. Pp. 532, with 146 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1953.

The author has taken previously published material and extended it for this volume. The first half contains rapid descriptions of disease entities; the second half approaches the subject of gynecology by discussing symptoms and their various significances. This arrangement has led to repetition, a good enough teaching principle but wasteful of space and leading to some disorganization in the text. No embryology or normal anatomy is given, and normal function is scarcely mentioned. The book is apparently designed as an introduction to the study of gynecology for the undergraduate student. The photographs and photomicrographs are excellent. The text is somewhat uncritical and presents the author's conclusions without argument and with little reference to the work of others. There are no descriptions of even minor surgical procedures; the irradiation techniques are not sufficiently well described to be used directly. Where results are reported, as in the treatment of malignant disease, the newest statistics are not included. A number of statements are made that will not find general acceptance. The book will probably be most useful as a supplement to the author's own undergraduate teaching activities. It is printed on good paper, and the subject index is detailed.

Developmental Psychology. By Elizabeth B. Hurlock, Ph.D., Associate in Psychology, Graduate School, University of Pennsylvania, Philadelphia. Cloth. $6. Pp. 556, with 62 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd Street, New York 36; 95 Farringdon Street, London, E.C.4, 1953.

A detailed outline of the changes that take place in human beings from conception to death is the principal content of this volume. In an easy and interesting style the entire developmental process is outlined for each age. Though this is essentially a treatise on psychology and the emotional and social changes accompanying each life period, there is also a brief but reasonably complete description of the changes in physical structure and functions that underlie the changes in psychological development.

After an introduction entitled "Growth and Decline," the general plan of the book is developed in chapters entitled "How Life Begins," "Infancy," "Babyhood," "Early Childhood," "Late Childhood," "Puberty," "Early Adolescence," "Late Adolescence," "The 'Mature' Adult," "Adulthood," and "Old Age." Within each of these physical development, motor skills, emotions, social behavior, interests, religious attitudes and behavior, sex interests and behavior, moral behavior, family relationships, and personality are discussed. Constant reference is made to the works of all of the principal authors in these fields. Supplementing the text is a list of visual aids, an extensive bibliography, and an index.

This book has been designed to give "as complete a picture of the developmental changes of the total life span of the human being as is possible within the two covers of one book." It is intended for use as a text or reference volume in university courses on developmental psychology. It would be suited not only for this purpose but also for a reference volume for physicians who are constantly dealing with people in all the age groups mentioned and who could check their observations of behavior with the observed norms set forth in this volume.

A Century of Medicine, 1848-1948: The History of the Medical Society of the State of Pennsylvania. Edited by Howard Kistler Petry, M.D. Cloth. Pp. 404, with illustrations. Medical Society of the State of Pennsylvania, 230 State St., Harrisburg, 1952.

This centennial history, covering the years 1848-1948, is more than just the interesting story of the birth, growth, and development of one of the nation's leading state medical societies. Because Pennsylvania, which often has been called "the birthplace of American medicine," can point to so many "firsts" in medical history, the book also reflects the nation's medical progress and the sweeping scientific, social, and economic changes that affected the practice of medicine during the past 100 years. Its chapters are studded with the names of physicians, medical educators, hospitals, medical schools, and other persons and institutions well known for their contributions to the advancement of American medicine. In addition to tracing the general history of the society, the book also has special chapters on the woman's auxiliary, the scientific sections, the county societies, permanent secretaries, publications, present functions and activities, and the centennial celebration.

Manic-Depressive Disease: Clinical and Psychiatric Significance. By John D. Campbell, M.D., Attending Psychiatrist, Georgia Baptist Hospital and St. Joseph's Infirmary, Atlanta. Cloth. $6.75. Pp. 403, with 2 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy Street, Montreal, 1953.

This manual for the general physician and psychiatrist discusses manic-depressive disease from a physiological viewpoint. It is a survey of the disease based on the study and follow-up of a group of 522 selected patients seen in the author's private practice. Following a historic review of manic-depressive disease, with emphasis on Kraepelin's description of the condition, Dr. Campbell presents his views on the nature of the disturbance and methods of treatment. The autonomic and emotional disturbances and mental symptoms of the disease occurring in the cycloid personality are described. A physiological disturbance of the autonomic nervous system is considered the causative factor, and conscious conflicts the symptoms. Environmental factors that upset the autonomic balance in a constitutionally predisposed person are considered by the author to be the precipitating agents. Other topics that are discussed in the book along with illustrative case material include manic-depressive disease in children and the social complications of the disease, such as marital problems, excessive use of drugs, homicide, and suicide. Treatment of the cyclothymic personality and mild manic-depressive disease includes removing aggravating en-

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These book reviews have been prepared by competent authorities but do not represent the opinions of any official bodies unless specifically so stated.

vironmental factors, using psychotherapy, aiding relaxation, and prescribing appropriate drugs. A review of the use of electroconvulsive therapy, electrostimulation therapy, psychosurgery, and current research theories of the nature of the autonomic disturbance in manic-depressive disease is included.

Problems in the Anatomy of the Pelvis: An Atlas. By Eduard Uhlenhuth, Ph.D., Professor of Anatomy, University of Maryland, School of Medicine, Baltimore. With assistance of DeWitt T. Hunter, M.D., Instructor in Anatomy. Cloth. $10. Pp. 206, with 82 illustrations by William E. Loechel, Medical Artist in Department of Anatomy. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

In this atlas the retrovesical space was selected as a focal point of discussion because of its importance in pelvic surgery. This is true because every subperitoneal space is related to the retrovesical space and every pelvic organ is in the immediate environment of this space. The presentation that relates the retrovesical space and the ureters is especially good. The "inferior hypogastric wing" received special consideration in order to stress its importance as a conduit of nerves and vessels and the part it plays in supporting the bladder and prostate gland. Although acceptable, the concept of the pubococcygeus, the puborectalis, and the iliococcygeus as the component parts of the levator ani might be objectionable to some anatomists. Other differences in opinion might arise in nomenclature.

The material presented is good although the method of presentation is unduly complex. The reviewer finds it difficult to look on one page where the structures are numbered and then to have to seek on an opposing page for the identification of the number and structure. It would have added much to this fine work had the artist and author synchronized their work so as to label each structure more directly. Particularly is this true of figure J 2 on page 125, where 40 structures have been numbered. It is a tiresome task to refer to the opposite page for so many identifications. This book should be useful as a reference to those who have acquired some knowledge of anatomy in their undergraduate courses. It can be recommended to graduate students, hospital staff members, surgeons, and anatomists interested in this region of the body.

A Ciba Foundation Symposium: The Spinal Cord. Editor for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B. Consulting editors: J. L. Malcolm, M.B., Ch.B., B.Med.Sc., and J. A. B. Gray, M.A., M.B., B.Chir. Assisted by Jessie S. Freeman, M.B., B.S., D.P.H. Cloth. $6.50. Pp. 300, with 112 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1953.

This book is the record of a symposium on the physiology of the spinal cord given at a meeting held in London from Feb. 26 to 28, 1952. The fifty or so participants included, among others, Adrian, Barron, Bremer, Bülbring, Creed, Dale, Eccles, Feldberg, Liddell, Matthews, Romanes, Skoglund, and Young. They surveyed the more recent advances concerning the functioning of the spinal cord. Of current clinical import there is little information save perhaps on the effects of various pharmaceutical agents on cord activity, which may conceivably be of value in dealing with spasticity. The large clear printing on nonreflective paper, the excellent diagrams, and author and subject index make a fine, compact volume that should be most useful to the neurophysiologist and to those doing clinical research in neurology.

Antibiotics. By Robertson Pratt, Ph.D., Professor of Pharmacognosy and Plant Physiology, University of California College of Pharmacy, San Francisco, and Jean Dufrenoy, D. Sci., Research Associate in Antibiotics, University of California College of Pharmacy. Second edition. Cloth. $7.50. Pp. 398, with 87 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1953.

This rather extraordinary volume covers the whole field of the antibiotics. Experimental work, the practical problems of production, the clinical use, and the philosophical implications of the advent of antibiotics are discussed. The presentation is somewhat marred by the use of technical jargon, as for example, "to biosynthesize" and "renal-ligated." Some inaccuracies are found primarily in the pages that deal with the clinical usage of the antibiotics. For example, it is stated that "the virtual lack of toxicity of penicillin . . . makes this antibiotic the drug of choice" in certain infections. It is hard to reconcile this statement with the known and increasing frequency of reactions to penicillin. The discussion of the use of priming doses of antibiotics is not in line with current thought. The lack of recognition of the rapid increase in the resistance of many micro-organisms to the antibacterial effects of streptomycin is surprising. These examples and others that appear in the clinical sections of this book give it a real unevenness. Although interesting, this treatise cannot be highly recommended to the practicing physician. It is much better written from the point of view of experimental and industrial developments relative to antibiotics.

Recreation for the Aging. Prepared for National Recreation Association by Arthur Williams. Cloth. $3. Pp. 192. Association Press, National Council of the Y. M. C. A., 291 Broadway, New York 7, 1953.

Prepared for the National Recreation Association, this well-written volume is a practical planning guide for those interested in recreational programs for older groups. It draws extensively from successful programs in action throughout the country and reveals thereby that an amazing number and variety of excellent, organized recreational group activities for the elderly are already in operation. The point of view and approach to the subject is sound in the light of present-day thinking. For instance, the author writes, "Inactivity is bad for the aging. The rest cure for old age has been discredited in favor of stimulating and vigorous activity suited to the capacities of the individual. If mental and physical deterioration is to be avoided, new interests and new goals must be found or old interests and aspirations rediscovered. . . . Recreation provides many opportunities for new personal contacts through which older folks can find escape from loneliness. . . ." Throughout the volume it is made clear that recreational activities, to be successful and worth while, must and can be something far more significant than merely "killing time."

Fourteen chapters are devoted to the organization and financing of recreation programs and the conduct of their various forms such as camping, arts, crafts, and hobbies. Other chapters discussed are recreation for special groups such as the handicapped, homebound, and institutionalized and for special agencies such as church, industry, and labor. There is a comprehensive bibliography and a complete index. There is more to this book than the title suggests. Anyone who has anything at all to do with recreation for older persons will benefit by reading it.

Hoppe-Seyler/ Thierfelder Handbuch der physiologisch- und pathologisch-chemischen Analyse für Ärzte, Biologen und Chemiker. Herausgegeben von Konrad Lang, Emil Lehnartz, unter Mitarbeit von Günther Siebert. Erster Band: Allgemeine Untersuchungsmethoden, erster Teil. Bearbeitet von F. Ender, et al. Tenth edition. Cloth. 185 marks; subscription price 148 marks. Pp. 762, with 502 illustrations. Springer-Verlag, Reichpietschufer 20, Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, 1953.

The five volumes that will make up the 10th edition of this famous handbook are being issued separately. The fifth volume on organs, body fluids, and secretions came out earlier in 1953 and was reviewed in THE JOURNAL (Sept. 12, 1953, page 177). Like volume 5, volume 1 is clearly written, logically organized, thoroughly indexed, copiously illustrated, and beautifully printed and bound. It should reach a wider audience than volume 5 because, in addition to its interest to the medical profession, the general methods that are covered here serve also as tools for research in physiological and pathological chemistry and because the individual monographs often are as good as the textbooks available to the general chemist. The methods that are included in this volume are: use of the polarizing microscope on crystals, micro methods including spot tests, electrophoresis, use of the ultracentrifuge, chromatography, counter-current extraction, microscopy, absorption and emission spectroscopy, nephelometry, refractometry and interferometry, polarimetry, and electrical conductivity. The last three chapters are on hydrogen-ion concentration (pH), colorimetric measurement of pH, and redox potentials. Each chapter has extensive bibliographies.

World Distribution of Dengue and Yellow Fever. Atlas of Distribution of Diseases—plate 5. Map reprinted from Geographical Review, vol. 42, no. 2, 1952. Paper. Pp. 14. American Geographical Society, Broadway at 156th Street, New York 32, 1952.

World Distribution of Plague. Atlas of Diseases—plate 6. Map reprinted from Geographical Review, vol. 42, no. 4, 1952. Paper. Pp. 7. American Geographical Society, Broadway at 156th Street, New York 32, 1952.

World Distribution of Leprosy: Leprosaria Shown on Map. Atlas of Diseases—plate 7. Paper. Pp. 20. American Geographical Society, Broadway at 156th Street, New York 32, 1953.

Study in Human Starvation: Sources of Selected Foods. Atlas of Diseases—plate 8. Paper. Pp. 2. American Geographical Society, Broadway at 156th Street, New York 32, 1953.

Study in Human Starvation: Diets and Deficiency Diseases. Atlas of Diseases—plate 9. Paper. Pp. 18. American Geographical Society, Broadway at 156th Street, New York 32, 1953.

These maps are a continuation of a series. Plate 5, "World Distribution of Dengue and Yellow Fever," shows areas of urban epidemics, sylvatic epidemics, and endemic areas of yellow fever; presents a table showing the distribution and habits of known vector species; and lists places where mouse protection tests for yellow fever immune bodies have been made on human beings in recent years. Epidemic and endemic dengue areas are also shown. Plate 6, "World Distribution of Plague," in addition to maps, presents a table showing the domestic and sylvatic rodent host and vector by countries. One insert map shows the length of the plague season in various locations. Plate 7, "World Distribution of Leprosy," shows the location of leprosaria and contains a table showing the number of known and estimated cases by countries (for the United States: 390 and 2,000 respectively). Plate 8, "Study in Human Starvation: Sources of Selected Foods," in addition to maps, contains a table showing the production of food animals, fish, cereals, and fruits; a table showing the food supply in grams per capita per day for various countries; a table of the composition of foods; and a table of the per cent of the total area in arable land and in pasture land by countries. Plate 9, "Study in Human Starvation: Diets and Deficiency Diseases," indicates the areas in which significant prevalence rates for the avitaminoses are found and areas in which diets are deficient in calories. The maps are well printed, easy to read, and contain notes on epidemiology as well as reference lists on the backs divided into basic sources and selected bibliographies by countries.

A Source-Book of Medical Terms. By Edmund C. Jaeger, D.Sc. Foreword by Irvine H. Page, M.D., Director, Research Division, Cleveland Clinic Foundation, Cleveland. Cloth. $5.50. Pp. 145, with illustrations by Lloyd Mason Smith and author. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

In this book have been assembled in alphabetical sequence the numerous word elements, combining forms, prefixes, and suffixes from which modern medical terms have been coined. Following each are the Greek, Latin, French, or other words from which it has been derived, together with the original meanings. For those readers who have had no training in Greek and Latin grammar, the various forms of nouns, adjectives, and verbs as well as related words needed to account for the complete spelling of the majority of terms employed in modern medical writing, are presented succinctly. With each entry numerous examples are offered to show how the word elements have been used in the construction of medical terms. These examples, taken from medical dictionaries, are dissected into basic formative elements. No medical dictionary has ever attempted this type of etymological treatment. In making readily available adequate information on the etymology of many medical terms, a distinct and helpful contribution is made. Because this book makes the origin and literal meanings of words clear to the inquisitive reader and tells of their application in special cases, as well as their history and how they happen to be spelled as they are, the information in this small book is of inestimable value to all who deal with the written and the spoken medical word.

A Primer of Cardiology. By George E. Burch, M.D., F.A.C.P., Henderson Professor of Medicine, Tulane University School of Medicine, New Orleans. Second edition. Cloth. $5.50. Pp. 339, with 214 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1953.

A perusal of this second edition indicates that it will create as much interest as the first. New material has been included and viewpoints changed without sacrificing the style that made the first edition popular. The section on congenital heart disease has been greatly expanded, and alterations appear in regard to the mechanisms of congestive failure and edema. The discussions of the treatment of congestive heart failure, coronary occlusion, and angina pectoris have also been expanded, and that of the treatment of syphilis has been brought up to date. Throughout, emphasis has been placed on the correlation of basic principles of cardiovascular physiology with clinical cardiac states. Controversy has been avoided, and the text has been profusely documented with illustrations. Occasional errors in proofreading mar the otherwise excellent presentation, e. g., figure 149 erroneously shows a diastolic pressure of 8 mm. Hg in the normal aorta, and, on page 248 when dealing with cardiac catheterization, the author states that an increase in left ventricular pressure occurred when obviously the right ventricular pressure was meant. These will doubtless be corrected in reprinting. In an era of a plethora of texts on cardiovascular disease, this primer will continue to make a prominent place for itself. It is highly recommended.

Inhalation Therapy and Resuscitation. By Meyer Saklad, M.D., Director, Department of Anesthesiology, Rhode Island Hospital, Providence, R. I. Publication number 156, American Lecture Series, monograph in Bannerstone Division of American Lectures in Anesthesia. Edited by John Adriani, M.D., Director, Department of Anesthesia, Charity Hospital, New Orleans. Cloth. $7.50. Pp. 343, with 110 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

In a world increasingly beset by industrial and automobile accidents and by military casualties, a thorough and practical book on resuscitation and oxygen therapy is greatly needed. In the treatment of the seriously ill patient, a clear understanding of anoxia is necessary. These needs have been filled by Dr. Saklad, who has had many years of experience in this and related fields. Conditions requiring oxygen therapy or resuscitation are considered from the physiological and pathological standpoint, and the causes, symptoms, and treatment are thoroughly explained on a practical level. The advantages and disadvantages of alternative procedures are discussed, and specific recommendations are made for various situations. The advantages and disadvantages, the best fields of usefulness, and the mechanisms of operation of the numerous devices for oxygen therapy and resuscitation now available are thoroughly explained. This work has an excellent outline, is clearly written, and contains many helpful illustrations.

The Obstetrical Forceps. By L. V. Dill, M.D., F.A.C.S., Head, Obstetrics and Gynecology, Yater Clinic, Washington, D. C. Publication number 150, American Lecture Series, monograph in Bannerstone Division of American Lectures in Gynecology and Obstetrics, edited by E. C. Hamblen, B.S., M.D., F.A.C.S., Professor of Endocrinology, Duke University School of Medicine, Durham, North Carolina. Cloth. $5.25. Pp. 156, with 86 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Illinois; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

This is the most recent addition to the obstetric-gynecologic contributions in the American Lecture Series. It does not report original contributions nor is there any evaluation of results. It is the sort of presentation that one might use to supplement a demonstration with an obstetric manikin or might make available to an intern for his clinical guidance. The use of all of the general types of obstetric forceps is discussed with detailed attention to the author's conclusions as to indications and application. It is in this particular field that the best portions of the book are found. There is a short chapter on fetal damage from forceps. The volume is printed on glossy paper and is satisfactorily illustrated with somewhat schematic drawings and with photographs. There is a subject index and a sketchy bibliography.

QUERIES AND MINOR NOTES

DUMPING SYNDROME

TO THE EDITOR:—*1. Does exercise or tension (anxiety, worry) cause hypoglycemia in a normal person or in a person with dumping syndrome? 2. How does coffee, tea, or amphetamine affect a person with hypoglycemia due to dumping syndrome? 3. Is the result of an intravenous glucose tolerance test abnormal in a patient with dumping syndrome?*

M.D., Ohio.

ANSWER.—Exercise, unless severe and prolonged, does not cause significant hypoglycemia in a normal person. Nervous tension commonly characterizes otherwise normal persons who experience "functional" hypoglycemia some hours after a meal (Portis and Zitman: *J. A. M. A.* **121**:569 [Feb. 20] 1943; Conn: ibid. **134**:130 [May 10] 1947). Relief is afforded by a low carbohydrate, high protein, and high fat diet, and possibly by atropine. The dumping syndrome consists of weakness, dizziness, flushing, warmth, perspiration, epigastric fulness, palpitation, and nausea, appearing immediately or within a few minutes after eating. The cause is believed to be sudden distention or irritation of the jejunum due to abnormally rapid emptying of the stomach. The syndrome is seen most frequently after gastroenterostomy or gastric resection, but has been described also in hypersensitive, overly reactive persons who have had no gastric operation (Alvarez, W. C.: *Gastroenterology* **13**:212, 1949). Hypoglycemia is not a necessary part of the dumping syndrome, but some patients with the latter condition, whether it is of surgical origin or not, experience hyperglycemia soon after eating, followed by a reactive hypoglycemia two or three hours later. Whether exercise further lowers the blood sugar in such cases is a question on which there is no direct evidence. Presumably it would if exertion were excessive. Whether nervous tension would exaggerate the hypoglycemia due to the nonsurgical dumping syndrome is a matter for speculation.

Coffee and tea have no appreciable influence on the blood sugar or the dumping syndrome. Amphetamine has little or no effect on hypoglycemia. In doses of 10 to 30 mg., it is said to delay gastric emptying (Ivy, A. C., and Krasno, L. R.: *War Med.* **1**:15, 1941). To the extent that this is true, the drug might be expected to retard the rapid discharge of food into the intestine, thus minimizing the excessive rise and fall of the blood sugar. Another review, however (Reifenstein, E. C., and Davidoff, E.: *New York J. Med.* **39**:42, 1939) points out that reports on the action of amphetamine on gastric motility are conflicting and that results vary according to original tonicity of the stomach. The result of an intravenous glucose tolerance test is not abnormal in a patient with the dumping syndrome.

GLUCOSE SOLUTION INTRAMUSCULARLY

TO THE EDITOR:—*Can from 2.5 to 5% glucose solution be given intramuscularly without causing sloughing? In what amount can it be given?* *H. E. Dester, M.D., India.*

ANSWER.—Glucose may be given intramuscularly in concentrations up to 5% without causing sloughing. The amount that may be given varies with the state of dehydration, circulation, and pain from distention and irritation. In dehydrated patients, glucose can be given in isotonic strength by hypodermoclysis in amounts up to 80 cc. per kilogram of body weight quite readily without undue distention of the tissues, especially when it is used with hyaluronidase. This is preferred when extravascular fluid administration is desired.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

FACE MASKS

TO THE EDITOR:—*Has anyone proved the value of face masks to prevent the dissemination of tubercle bacilli? In our hospital small cellulose masks are worn by the patient and visitors. I would appreciate references on this subject.*

John C. Meyers, M.D., San Francisco.

ANSWER.—The permeability of face masks depends on such factors as the tightness of the mesh, the size of the holes, the number of holes per square centimeter, and the speed of the droplets. The common operating room mask of two layers of gauze with a heavy layer of cotton flannel between will retain most bacilli and droplets of moisture with ordinary breathing, but explosive coughing will probably drive a few bacilli through the openings. The openings in the mesh of cotton flannel are minute, and the air pathway through the mask is devious, so that particles are almost sure to be caught on the cotton fibers. Tight cellulose masks are better in some respects and are fairly safe for all ordinary purposes. The holes are smaller and farther apart. Jennings (*Am. Rev. Tuberc.* **32**:304, 1935) showed that one thickness of a cellulose paper napkin was nearly as effective as 10 thicknesses of ordinary gauze. The openings are not one-tenth the size of those of the woven gauze. The culture experiments roughly parallel the aggregate size of the openings.

Obviously, the problem of the safety of masks is a relative one. No mask will ever be made through which a few bacilli may not be driven with explosive coughing, but if 95% of the bacilli are held back the danger will be greatly reduced. Only the smallest droplets will pass through, and these contain small doses of bacilli that will infect fewer persons than the large clumps thrown out in an uncovered cough. The Curity mask with a pliable nose piece is probably one of the best masks for all purposes. It is a specially tightly woven filter fabric of cotton flannel covered on both sides by fine mesh gauze, with tapes and flexible metal nosepiece. It is made to fit the face and gives comfort and fits tightly against the nose, cheeks, and chin. No mask should be worn until it is too moist, and they should be changed often and washed and sterilized with great care.

ULTRAVIOLET LIGHT

TO THE EDITOR:—*Kindly tell me the current opinion about the use of ultraviolet light in the nasal and oral cavities. In what diseases could it be of value? Would a nasal application giving off ultraviolet radiation be of any practical value? What would be a safe dosage, if any?*

Seymour B. Jacobson, M.D., New York.

ANSWER.—Ultraviolet light for use in the oral and nasal cavities does not seem to be as popular at present as it was some years ago. It has been reported that the local application of ultraviolet light may serve as adjunctive therapy in the treatment of nasal and oral tuberculous lesions. In some cases, it is also useful as adjunctive therapy in the management of infected wounds, septal ulcers, and certain oral dermatoses. The value of its use in the treatment of hay fever has not been convincing, and the use of ultraviolet radiation for nasal sinus infections is practically of no value because it is unable to reach the sinuses involved. The inability of ultraviolet light to penetrate through a thin pyogenic membrane further detracts from its value. There is a tendency, in the case of local application of ultraviolet light, to damage tissue as well as bacteria with the resulting possible necrosis of normal tissue.

It is customary to apply local ultraviolet radiation by means of the water-cooled quartz mercury vapor lamp (Kromayer lamp) wherein a quartz rod applicator is placed near the lesion. Since, because of the proximity of the applicator to the subject, it is impossible to apply intense amounts of ultraviolet energy, short exposure times are required. The dosage for the Kromayer lamp is determined by a slight modification

of the usual cutaneous test for determining the minimal erythemal dose. The minimal erythemal dose is determined by exposing small areas of the forearm, through holes in a patch test cuff, for varying periods of time. In the case of Kromayer type lamp, an exposure of 5 seconds in a person of average skin pigmentation is the maximal time usually used for this test. The erythema can be expected to develop between 12 and 24 hours after this exposure. The time needed for the least perceptible erythema to develop is considered the minimal erythemal dose for the particular lamp tested when operated at the same distance from the patient. In applying radiation it is desirable on initial exposure to use a dose that is a fraction of the minimal erythemal dose. Subsequent exposure times are increased.

DIARRHEA IN DIABETICS

To the Editor:—*For 20 years a 65-year-old man has had diabetes, which is well controlled with 40 units of protamine zinc insulin daily. His general condition is good, and there are no significant complications. In the past six years he has had alternating constipation and diarrhea, being constipated for from four to six days and then having diarrhea for from two to four days. The diarrhea is often of such severity that he becomes prostrate. Various clinics and many internists and radiologists have failed to reveal any intestinal lesion. Stool examinations have never revealed blood, pus, mucus, ova, or parasites. All treatment to date including large parenteral doses of vitamin B_{12} has been of no avail. Have you any suggestions on therapy?*

Lewis R. Elias, M.D., Montgomery, W. Va.

Answer.—Nocturnal diarrhea usually occurs in younger diabetic patients, but in Joslin's series of 96 cases, the ages varied from 20 and 79 years and the average duration of the diabetes was 9 years. In the series reported by Joslin and associates (Treatment of Diabetes Mellitus, ed. 9, Philadelphia, Lea and Febiger, 1952, pages 485 and 486) and Rundles (*Medicine* **24**:111, 1945; *Bull. New York Acad. Med.* **26**:598, 1950) constipation alternated with diarrhea. Previous poor diabetic control was outstanding in each instance, and diabetic neuritis preceded the diarrhea in 40 patients. One of the most definite diagnostic points was the high level of total protein in the spinal fluid, averaging 88 mg. per 100 cc. in 17 of 18 cases. What was the total protein level in the spinal fluid of this patient? Did he have pernicious anemia? Was free hydrochloric acid present in his gastric secretion? Was the serum amylase level normal? Was there evidence of impaired digestion of fat and an excess of muscle fiber in the feces? Invariably the search should be pressed for organic causes. The only treatment that has been found at all helpful, besides the low residue, nonirritating diet, has been crude liver extract given parenterally. The injection of from 2 to 4 cc. of the extract daily for a few days, followed by a maintenance dose of 1 or 2 cc. weekly, usually proves adequate. Lapses in treatment are usually followed by a relapse of diarrhea, according to the Joslin report.

OTOSCLEROSIS

To the Editor:—*A woman, aged 36, has had progressive loss of hearing and tinnitus aurium for a year. Thorough examination fails to reveal any abnormality. At the onset she was anemic but with liver therapy her blood returned to normal. The eustachian tubes have also been intubated and inflated and injections of Jacobson's solution and high vitamin and high protein diet given. I see no improvement with all this therapy, and the patient states that the symptoms are as bad if not worse. What will alleviate this condition?*

Daniel Burman, M.D., Bronx, N. Y.

Answer.—Bilateral progressive loss of hearing with marked tinnitus in which examination of the ears reveals normal tympanic membranes and eustachian tubes and which all treatment fails to improve usually means otosclerosis. Inasmuch as any known therapy is useless, if the deafness progresses to so much that normal conversation is irksome at a distance of 2 or 3 ft., a hearing aid should be prescribed and the study of lip reading instituted.

BLOCKED FALLOPIAN TUBES

To the Editor:—*A patient has fallopian tubes that will not open under a pressure of 200 mm. Hg. She has no history of infection and has had one pregnancy, which ended in miscarriage. Should surgical opening of the fallopian tubes be attempted in her case?*

Ursula G. Mandel, M.D., Los Angeles, Calif.

Answer.—The failure of gas to pass through the fallopian tubes at a pressure of 200 mm. Hg does not necessarily mean organic tubal blockage. Tubal spasm may prevent the passage of gas. The Rubin insufflation should be repeated after the patient has received an antispasmodic drug such as glyceryl trinitrate (Nitroglycerin) 1/100 grain (0.6 mg.) parenterally. If the gas fails to pass through the tubes after this procedure, the uterus and tubes should be visualized by a radiopaque oil. This should be injected under fluoroscopic and pressure control. It is possible to see the uterus and tubes filling and to note the escape of oil from the ends. In any event, a roentgenogram should be made 24 hours later. If no oil is smeared amongst the pelvic viscera, the patient probably has tubal blockage; its location should be apparent in the roentgenograms made at the time of oil injection.

The surgical relief of tubal blockage is a specialized procedure that should be carried out by persons with an interest and training in sterility problems. The results obtained depend on the location of the obstruction, the extent of the tubal disease, the patient's age, and the fertility of her husband. Under ideal circumstances no more than one out of three patients subjected to salpingostomy conceives and has a baby. Various procedures have been devised to maintain patency of the tubes after they have been opened. In patients in whom the obstruction is at the uterine cornu, the tube may be severed from the uterus and implanted into the uterine cavity, through a new opening. Here a plastic tube inserted into the tube and uterine cavity is used to maintain patency. Although the results of tubal surgery have improved tremendously, patients should be selected carefully for these procedures.

X-RAY STERILIZATION OF OVARIES

To the Editor:—*My x-ray machine with the factors of 85 kvp, 25 ma., and 25 in. distance with a filtration equivalent to 1.5 mm. of aluminum gives 46 r per minute measured in air by a Victoreen meter. A roentgenogram of the pelvis is made with the same setup of factors but the exposure lasts 1½ seconds, thereby giving 1 1/6 r. How many pelvic roentgenograms such as this can be taken without exceeding the sterilization dose of the ovaries?*

M.D., California.

Answer.—There is no fixed value for the sterilization dose of the ovaries. A dose to the ovaries of 450 r given in one day or 600 r given over a period of two days will cause sterilization in most women. However, much smaller doses will produce sterilization in some women. Even smaller doses may not produce permanent sterilization, but result in amenorrhea of several months' duration. With the technical factors of the x-ray treatments outlined in the question, the number of roentgens reaching the ovary in an average-sized patient, per exposure, would be less than 0.4 r. It should be very difficult to produce permanent sterilization with x-rays of this quality. Severe skin reactions would be apparent before the sterilization dosage is reached. It should be added, however, that genetic damage, without sterilization, may result from very small doses of x-rays.

Answer.—The delivery of 400 r to the ovary in a single dose or a total of 1,000 r in a period of one week may be expected to produce sterilization in approximately 80% of cases. Under the conditions stated above, it is estimated that in a patient of average size the ovary would receive 0.25 r during the making of an x-ray film. This means that it would require the making of 1,600 pelvic films in a single day, or 4,000 films distributed over a week in order to deliver a dose that would accomplish sterilization in 80% of cases. Entirely aside from the matter of sterilization, there are excellent reasons for avoiding unnecessary radiation of any amount to any part of the body and particularly to the gonads.

WHISTLING NOISE OVER TEMPORAL AREA

To the Editor:—*I and some of my neurosurgical colleagues feel that a more accurate reply is required to the query on page 774 of* The Journal, *June 20, 1953, entitled, "Whistling Noise Over Temporal Area." The answer states, "The bruit alone would hardly be sufficient reason to make an angiogram or to consider any surgical treatment of this lesion." I take strong exception to this, as a bruit is one of the cardinal signs for an angiogram and prompt surgical intervention if it is possible. I say this because a bruit indicates a vascular fistula, which may rupture at any time and lead to a fatality. We also know that most arteriovenous fistulas or aneurysms tend to enlarge with time and may become inoperative by the time neurological abnormalities develop. I think you will find that almost every neurosurgeon today would agree that a bruit is definitely a reason for prompt cerebral angiography and surgical intervention if the lesion is in a suitable position for surgical treatment. May I conclude by saying how much I enjoy your section on Queries and Minor Notes.*

J. Lawrence Pool, M.D.
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New York 32.

TETANUS

To the Editor:—*I would like to comment on the answer to the Query and Minor Note on tetanus in* The Journal, *Aug. 22, 1953, page 1677. The answer states "if the possibility of tetanus infection is present." Actually there is always a possibility of tetanus infection, even from a scratch. From this standpoint, in an active pediatric practice a physician could be giving antitoxin all the time. Therefore, I give all my patients tetanus toxoid with booster doses every two to three years to keep up their basic immunity; in case of an injury a booster dose is given, which raises the titer rapidly. I still think tetanus antitoxin is unnecessary when a person has a proper antitoxic titer from his active immunization unless the injury is very severe. I believe active immunization is a lot safer than reliance on antitoxin. The prime reason for keeping up an active immunity is to obviate the necessity of giving either horse or bovine antitoxin and sensitizing the patient to serum.*

Douglas P. Arnold, M.D.
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Buffalo, N. Y.

EXCRETA FROM TOILETS ON TRAINS

To the Editor:—*A student handed me a clipping from* The Journal *of July 18, 1953, because of a query with reference to excreta from toilets on trains. We have been interested in the problem in an academic way because we are at a loss to explain the incidence of the cyst stage of the beef tapeworm of man, which seems to be higher in this region than in the more western regions with which I am familiar. It would be difficult to ascribe this higher incidence to any peculiar customs of the farmers themselves. Actually the sanitary conditions and habits about the farms in New York seem to be much better than in many other areas of the country. When the many Sunday drivers, picnickers, and hunters find it necessary to defecate, they tend to seek the privacy of bushes, which reduces the possibility of cattle coming in contact with fecal matter. On the other hand, trains tend to run in valleys, and the flat land in those valleys is often used by the dairy industry. The cattle are pastured along the rights of way, and feed is cut from these meadow areas. The point of all this is that we should not overlook the railroad as a mechanism in the spread of Taenia saginata from man to cow.*

I think it is important to look at the problem, not from the standpoint of fecal contamination per track mile, but from the standpoint of probability of fecal contamination per specific mile. Passenger trains are not distributed at random throughout the United States; nor are their times of arrival and departure from the metropolitan areas a matter of chance. Generally the Pullman trains are scheduled to leave in the evening for arrival at their destination in the morning. Human habits being what they are, I would hazard a guess that passenger contamination of the tracks from Pullman cars is much more likely to take place in an area of say 50 miles outside of a metropolis.

Furthermore, it does not seem fair to place all the responsibility for track contamination on the passengers. Railroads have train crews and section gangs. I have ridden in at least one caboose that did not have a toilet. There are many railroads whose primary job is hauling freight and that carry few passengers. Including such lines in the statistics is apt to be misleading. If the railroads present any sanitary problem at all, it is apt to be localized near the large cities, because not only the contamination from the Pullman trains is greater but also the probability of commuter and employee contamination is increased.

In summary then, I would first suggest that any figures based merely on passenger traffic are apt to be deceptive. The employee contamination must also be considered. Secondly, the distribution of railroads and passengers is not random, so any average statistic is very suspect. It is highly probable there are areas of especially great contamination. Thirdly, in examining for areas of contamination, the beef tapeworm of man is a factor to consider.

D.V.M., New York.

VECTORCARDIOGRAPHY

To the Editor:—*In* The Journal, *Nov. 7, 1953, page 992, in answer to a question on vectorcardiography, it was said that an approximate frontal plane vectorcardiogram could be constructed from the three standard leads and the three aV leads. May I point out that in the third edition of my book, "Unipolar Lead Electrocardiography and Vectorcardiography" (Philadelphia, Lea & Febiger, 1953), I describe very simple methods by which frontal, horizontal, and sagittal plane vectorcardiograms can be constructed with great accuracy, using only two electrocardiograms, namely, leads 1 and aVF for the frontal plane vectorcardiogram, leads 1 and V_1 for the horizontal plane vectorcardiogram, and leads V_1 and aVF for the sagittal plane vectorcardiogram.*

Emanuel Goldberger, M.D.
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New York 21.

TRICHOMONAS VAGINALIS

To the Editor:—*I have noted suggestions in Queries and Minor Notes for various types of treatment of Trichomonas vaginitis. None of these have mentioned the use of copper sulfate. I have found that one douche of copper sulfate, using 1 to 2 gm. to a liter of water, will relieve all symptoms; if the douche is repeated daily for several weeks, permanent cure will result in most cases. This simple method, in my experience, has been the best treatment for this condition.*

H. M. Purcell, M.D.
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Phoenix, Ariz.

BURNING PAIN IN FOOT

To the Editor:—*In* The Journal, *Oct. 17, page 693, is a query about "burning pain in foot." I find this symptom present in early osteoarthritis, and generally treatment with 2.5 to 4 gm. of sodium salicylate gives relief. In patients that do not respond to sodium salicylate, I have found that 50 mg. of tripelennamine (Pyribenzamine) or a similar antihistaminic given three or four times a day has given relief. These simple measures can be used for patients of any age.*

Charles R. Svoboda, M.D.
Chapman, Kan.